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[Official history of the war]:

HISTORY OF THE GREAT WAR

BASED ON OFFICIAL DOCUMENTS.

MEDICAL SERVICES.
DISEASES OF THE WAR.

VOL. I

Edited by
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CONTENTS.

CHAPTER PAGE

List of Contributors v

Preface vii

I. General Aspects of Disease during the War 1

II. Enteric Group of Fevers 11

III. Dysentery 64

IV. Cholera 116

V. Typhus Fever 133

VI. Cerebro-Spinal Fever 147

VII. Influenza 174

VIII. Purulent Bronchitis and Broncho-Pneumonia 212

IX. Malaria : Ætiology, Incidence and Distribution .. 227

X. Malaria (*contd.*) : Pathology, Symptoms, Diagnosis and Treatment 264

XI. Blackwater Fever 294

XII. Trypanosomiasis 305

XIII. Relapsing Fever (Spirochætosis) 316

XIV. East African Relapsing or Tick Fever 329

XV. Phlebotomus Fever 345

XVI. Trench Fever 358

XVII. Jaundice 374

XVIII. Scurvy 409

XIX. Beri-beri 430

XX. Famine Dropsy 450

XXI. Pellagra 470

XXII. Nephritis 485

XXIII. Cardio-Vascular Disorders 504

Index 539

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LIST OF COLOURED PLATES.

PLATE		TO FACE PAGE
I.	Cerebro-spinal Fever :
	Erythematous Rash (Fig. 1)	152
	Petechial Rash (Fig. 2)	152
II.	Cerebro-spinal Fever :
	Macular Rash	154
III.	Cerebro-spinal Fever :
	Purpuric Rash	156
IV.	Influenza :
	The "Heliotrope Cyanosis" of Influenzo-pneumonic Septicæmia	180
V.	Influenza :
	Whole Lung in a Case of Influenzal Pneumonia . .	198
VI.	Jaundice :
	Right Lung from a Case of Spirochætal Jaundice (Ictero-hæmorrhagica)	392

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Note.—(T) means temporary commission.
(T.F.) means Territorial Force commission.

PREFACE.

THE chapters of the volumes on the Diseases of the War have been prepared by officers who held regular, territorial force or temporary commissions in the Royal Army Medical Corps, and who had special knowledge and personal experience of the diseases about which they write. The material contained in official documents, supplemented by the numerous references appended to each chapter, has been at their disposal.

In the present volume a considerable amount of repetition will be found, notably in the chapters on influenza and purulent bronchitis, consequent upon these diseases having been considered from two separate standpoints, namely, the experience of the epidemic amongst the troops in France and the experience of the epidemic in the United Kingdom.

The second volume will contain chapters on nervous disorders, venereal and skin diseases, in addition to chapters on the medical aspects of aviation, gas warfare, and mine gas poisoning. Although these latter subjects have a wider significance than that of actual disease and might of themselves have formed a separate volume, it has been found convenient to introduce them into the volumes on the Diseases of the War.

The measures for preventing disease, and the methods and results of laboratory research are fully detailed in the volumes which will be published separately on Hygiene and Pathology during the War, and reference must be made to them for fuller information on these subjects. But it has been considered advisable to introduce a certain amount of detail with regard to preventive treatment and pathology into the present volumes.

It has been preferable, in an historical record such as this, to adopt the form in which the subjects are now presented rather than the form which is customary in text-books or articles in journals. The chapters are based chiefly on such work as was done during the progress of the war. There has been little opportunity for further analysis and study of the accumulated records of medical cases. Consequently the final nature of the invalidism produced by the various diseases has not been described with that measure of accuracy which can only come when the documents now in the hands of the Ministry of Pensions are analysed in detail. Moreover, even in respect of dealing with actual clinical experience, the contributors to the present volume have been handicapped by the fact that papers published during the war were comparatively few. This restriction of papers and consequently of clinical and pathological studies was due to the general military policy which of necessity governed the publication even of medical reports.

The chief work of editing the chapters has been carried out by Major-General Sir Wilmot Herringham, Colonel T. R. Elliott, and Lieut.-Col. Andrew Balfour, who have devoted an immense amount of valuable time and care to doing so. They desire to acknowledge the able assistance which they received from Major T. J. Mitchell, R.A.M.C., and the staff employed in the office of the Medical History of the War.

Acknowledgments are also due to the *British Medical Journal*, *Journal of the Royal Army Medical Corps*, *Lancet*, *Quarterly Journal of Medicine*, the Medical Society of London, the Royal Society of Medicine, the Medical Research Council, the Cambridge University Press, and Messrs. Baillière, Tindall and Cox for permission to use blocks of various charts, illustrations and coloured plates, which have already appeared in their publications.

W. G. M.

CORRIGENDA.

(1) P. 12, Table I. France 1916: The correct number of cases is 2568, not 2668 as printed.

(2) P. 56, Line 14: The correct date is January, 1916, not January, 1915, as printed.

(3) Plates facing pp. 194 and 200 should be marked Figures 1 and 2, instead of Plates III and IV as printed.

DISEASES OF THE WAR.

CHAPTER I.

GENERAL ASPECTS OF DISEASE DURING THE WAR.

DURING war popular attention finds its chief interest in the number of the wounded, and concerns itself much less with the amount of sickness amongst the troops, although in every war of which we have records from the days of Sennacherib onwards the inefficiency from disease has outnumbered many times the losses from killed and wounded. Medical science has advanced so much that the figures of wars fifty and sixty years ago afford no useful bases of comparison. Those of the last two great wars are as follows :—

	Annual Ratio per 1,000.			
	Wounded.		Sickness.	
	Admissions.	Deaths (incl. killed).	Admissions.	Deaths.
South Africa, 1899–1902 (31 months).	34·2	14·4	843·0	24·58
Manchuria, Russo-Japanese War, Japanese Force, 1904–1905 (18 months).	391·6	137·3	589·6	41·2

The ratios in the table below are the total sickness rates and are calculated in the same way as those of the South African and Russo-Japanese Wars.

Year.	France.	Italy.	Macedonia.	Egypt & Palestine.	Mesopotamia.	East Africa.
1915	—	—	—	—	—	—
1916	—	—	982·7	618·7	1409·7	—
1917	—	—	837·9	745·2	1301·3	1403·5
1918	533·1	670·8	1011·7	1000·1	980·9	2310·6

But these figures do not indicate the proportion of sick and wounded, and for comparing them the actual admissions in certain years are as follows :—

	Wounded.		Sickness.	
	Total Admissions.	Total Deaths (incl. killed).	Total Admissions.	Total Deaths.
France, 1918 ..	574,803	46,084	980,980	8,988
Egypt and Palestine, 1917-1918	32,255	9,451	359,855	3,360
Macedonia, 1917-1918	12,552	2,843	331,753	3,031
Italy, 1918 ..	4,671	470	54,626	661
Mesopotamia, 1916–1918 (White troops only)	16,793	6,752	242,159	2,752

These figures show that the admissions for disease in other theatres than France were 14·6 times as numerous as those for wounds (988,393 : 66,271), while even in France, though the perfection of instruments of warfare and the constant fighting greatly increased the number of wounded, the admissions for disease were still much the more numerous. It was indeed anticipated that the disproportion would be even greater. The admission rates for sickness per 1,000 of strength in 1909, a year of peace, are given as :—

In the United Kingdom	378·4
In Egypt	672·9
In West Africa	1026·1

Further, in the Royal Army Medical Corps Training Manual published in 1911, it is stated that in wartime the excess of sickness admissions over those for injuries received in action will probably be as twenty-five to one, and that though the fatality of injury is greater than that of disease, the deaths from disease are usually five times the more numerous.

To the mere statement of numbers given above three other factors should be added before the effect of wastage from disease during the war can be realized, namely, the average number of days that patients remained in hospital, which in France was found to be 45*, the cost of transport and maintenance of the patient, and the cost of the training and transport of the man sent up to take a patient's place in the ranks.

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* But this average refers only to those cases treated and discharged in France. Many of the severer cases were transferred to England, and these probably took much longer to convalesce. Thus cases of dysentery treated

These considerations are sufficient to show the importance of disease as a cause of inefficiency in an army, and the vast expense which it entails upon the country.

The natural circumstances of each country differ so widely that the prevalence of diseases varied much in the different theatres of the war, as is shown in the following table.

Rates per 1,000 of strength.

	France.	Italy.	Macedonia.	Egypt & Palestine.	Mesopotamia.	East Africa.
Enteric—						
1915	3·1	—	—	—	—	—
1916	2·3	—	6·3	14·2	54·4	—
1917	·7	—	2·5	·7	14·2	4·76
1918	·2	1·48	·8	·9	6·3	6·80
Dysentery—						
1915	·03	—	—	—	—	—
1916	4·09	—	63·89	31·19	50.94	—
1917	3·76	—	28·89	23·13	60·34	486·56
1918	·79	9·54	58·23	21·80	51·12	116·51
Malaria—						
1915	—	—	—	—	—	—
1916	·05	—	331·47	8·10	68·61	—
1917	·48	—	353·18	44·66	94·20	2880·9
1918	1·77	2·90	369·29	134·40	95·79	1278·0
Nephritis—						
1915	7·16	—	—	—	—	—
1916	8·46	—	—	—	—	—
1917	9·51	—	—	—	—	—
1918	4·17	—	—	—	—	—

The enteric rate of admissions was nowhere over 10 per 1,000 of strength except in Egypt during 1916, and in Mesopotamia during 1916 and 1917. Dysentery was very prevalent in East Africa, Egypt and Mesopotamia. Malaria was exceedingly prevalent in East Africa, Macedonia and Egypt. Its great prevalence in Macedonia in 1916, and in Egypt in 1918, coincides with the advance into the infested valley of the Struma and plain of Esdraelon. This distribution was on the whole expected from previous experience.

Nephritis is not mentioned in other statistics than those of the forces in France, where it formed an appreciable item, nor was trench fever made a notifiable disease elsewhere, though it was

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in France averaged 42·3 days under treatment, while those which were transferred to England averaged 118·3 days. The 45 days mentioned in the text is much less than the average number of days for all cases of illness contracted in France.

seen in Macedonia after divisions had gone there from France.

Although a war carried on in many areas and climates cannot be closely compared as a whole with previous wars confined to one country, the admission rate for sickness in France in 1918 (533·1 per 1,000 of strength) compares favourably with those of the South African War (843·0) and the Russo-Japanese War (589·6). The climatic conditions in Manchuria were favourable to health, and Japanese sanitary methods as regards cleanliness of person and sanitary discipline were extremely good. Most of the Japanese sickness was due to beri-beri, from deficiency of vitamine in their ration, the chief constituent of which was polished rice. On the other hand, however, if there were in France, in the wet climate and in the conditions of trench warfare, factors unfavourable to health, there were also in the absence of extreme temperatures and of endemic disease, in the shortness of the lines of communication and the consequent abundant supply of food, and in the facilities for sanitation and early treatment of illness, points which might be expected to tell heavily on the other side.

In other theatres of the war the sick rate was very much heavier. On the whole, a more favourable theatre than France could hardly be expected, and while an improvement on the Japanese figures may be regarded as eminently satisfactory, it is necessary to inquire whether in France the results could not have been better, and why in other countries they were much worse than the Japanese ratios. This is all the more necessary since of the epidemic diseases which are known to have been the scourges of previous campaigns—dysentery, malaria, enteric, smallpox and typhus—the last two have been practically absent amongst the British troops, and enteric was very much less prevalent than in any previous war.* Nor was there any disease, except malaria in certain theatres of war, which caused the same amount of inefficiency as beri-beri did in the Japanese armies.

The extraordinary improvement in the figures for enteric fever as compared with those in the South African War is remarkable. During the 31 months of the South African War, in which ration strength was probably never more than 250,000, there were 59,750 admissions for enteric, with 8,227 deaths. During 53 months of war in France, during which the ration strength rose from 269,711 in 1914 to 2,528,400 in 1918, the total number of admissions for enteric fever, including typhoid and the para-typhoids, as noted in Chapter II, was 6,907, and the number of deaths 260. Since enteric was prevalent among the civilians in the area which the British occupied during 1915, and since the French troops had a large number of cases up to the time at which they altered their system of prophylactic inoculation, it is fairly certain that the British troops would have been attacked but for the three measures specially designed to prevent it: the prophylactic inoculation, the strict water control, and the vigilant search for "typhoid carriers." The great improvement in the French figures which followed on the alteration of their system of inoculation is evidence that this measure played an important part. The small incidence of enteric was not confined to the expeditionary force in France. Except in Mesopotamia and in Egypt during 1917 the rate nowhere rose to double figures, and in every area except East Africa it sank lower year by year.

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* In France, during 1914–1918, there were only eleven cases of smallpox, none of typhus. In Italy, in 1918, there were two cases of smallpox and none of typhus. The only theatres of war where there was any degree of prevalence of smallpox or typhus were Egypt, Palestine and Mesopotamia. Details regarding the former will be found in the volumes on the hygiene of the war, and regarding the latter in the chapter on typhus in this volume.

The same cannot be said of dysentery. In France the admissions for this disease did not reach any large total, but in other parts of the world, notably in East Africa, they rose to very high figures. These facts may indeed be used as evidence of the effect of inoculation as a preventive of enteric, for the channel of infection is the same in both diseases, the same sanitary precautions were taken for both, and in both the affected men were separated as quickly as possible from the healthy. But on the one hand the diagnosis of dysentery is more uncertain, so that segregation is more difficult, and on the other there is no prophylactic yet discovered for it. A lesson may be learnt, however, for the future. In France the diagnosis of dysentery was at first based upon bacteriological evidence alone. It was soon found that in a large number of cases the bacilli were not recovered and accordingly the presence of blood and slime in the motions were regarded as sufficient evidence for a diagnosis. But cases showing these symptoms in the trenches might show simple diarrhœa by the time they reached the casualty clearing station, and in that event, in spite of orders to the contrary, the diagnosis was not infrequently altered, although, as the subsequent course of the case in base hospitals showed, the original diagnosis of dysentery was correct. If wastage by dysentery is to be reduced in future, it is of the utmost importance to segregate all infected men at the earliest possible time, and it should be clearly understood that medical officers should strive not to minimize the number of cases or to refuse all but the most rigid proof, but rather to watch for and at once discover and segregate all cases which may fairly be suspected. An army will lose far fewer men eventually by adopting this procedure.

The figures for malaria in Macedonia, Egypt, and Mesopotamia were not much more satisfactory, while in East Africa they were so excessive that an official enquiry into the causes was instituted. Although there may have been failure on the part of individual administrators, the questions of interest in the present connection are the deficiencies in existing knowledge, the limits which circumstances must sometimes set to the application of such knowledge as exists, and the means, if any, whereby, in the future, methods of prevention may be increased and treatment improved. The life history of the infection of malaria is of course known, and the building of the Panama Canal is evidence of what can be accomplished in the prevention of insect-borne disease when conditions admit of the necessary measures. But measures such as would be taken in Panama cannot be carried out in actual warfare. If troops are pushed forward into infected areas, destruction of breeding places may in some kinds of country be quite impossible, and almost equally impossible may be the protection of the soldier in the open while on sentry duty or in advanced posts, and even perhaps in bivouac, tent or billet. It is generally allowed that quinine is of little use as a prophylactic in war time, and it must be recognised that the occupation of a malarious area will inevitably cause a high malarial sick-rate.

In considering the possibility of a long campaign in an area such as that of Macedonia, it must be realised that at present the medical services cannot control the outbreaks of malaria, which are bound to occur, and that to occupy a malarial district for long will be as serious a drain on the strength of an army as to hold a shell-swept front, such as that of the Ypres sector in France. Moreover, the price of malarial casualties continues to be paid for many years after the campaign itself. In the autumn of 1920 malaria was still responsible for 13 per cent. of the total number of men drawing pensions for disabilities due to diseases contracted in the war, and was indeed the chief source of all the chronic forms of disability.

The history of scurvy in Mesopotamia is interesting from several points of view. In the first place its incidence brought to light the fact that the ordinary peace diet of the Indian soldier, which was provided by himself out of a money allowance and not as a Government ration, lacked many essentials of a scientific dietary, so that many of the men who arrived in Mesopotamia were noticed from the first to be anæmic, debilitated and below the proper level of health, and were liable to feel at once the slightest further deprivation which difficulties of communication might entail. In the second place, it is clear that the earlier war ration was not sufficient to overcome this tendency ; it, like the peace diet, had no surplus value available. Thirdly, the outbreak of the disease revealed that the remedies on which reliance had been placed, namely, dried vegetables and lime juice, were practically useless, whereas the really efficient substances, whether of old standing such as orange and lemon juice, or lately* discovered such as germinating pulses, were not available. Lastly, it is worthy of note that these commodities were eventually obtained, and also that by means of Arab and Indian gardeners a large amount of green vegetables was produced in the country.

But, after all, these infections count for little in the total sick-rate. It took a long time to realize that when the serious maladies were held in check it was time to attend to the minor diseases that made up the great total of wastage. In France a list of 21 diseases including all the eruptive fevers, together with the diseases just mentioned and some others, only accounted for 27·51 out of a total rate of 533·1 for 1918 ; in Mesopotamia in 1918 the dysentery and malaria rates amounted to 146·91 only, out of a total of 980·9 ; in Macedonia dysentery, malaria, and pneumonia with influenza made an aggregate rate of 538·85 out of a total rate of 1,011·7.

There are no official statistics as yet available to show what diseases constitute the remainder. A series of figures, however, was obtained from the casualty clearing stations of one of the armies in France during 1917, and was analysed by Colonel Soltau. The admissions numbered 106,267. As the total sick admissions for all the armies in France for 1917 are not known it is not possible to say what proportion Colonel Soltau's figures bear to the whole ; but they are little more than 10 per cent. of the total for 1918. Nor is it possible to compare his figures with the rates given above, since the strength of the army to which his figures refer is not available. But Colonel Soltau compares various diseases and classes of disease with one another under eight groups, and produces the following results :

Group " A ", which includes scabies, skin diseases, boils, and cases classed as inflammation of connective tissue, accounts for 26,879 of the admissions. " The main fact that emerges from a study of group ' A ' is that some 25 per cent. of the sick wastage was due to simple skin lesions, that of them the vast majority were due to scabies or some form of pyodermia, and as such were very largely preventible by careful inspection and personal cleanliness of the men, and that even where infection was established, prompt treatment was efficacious in greatly reducing the loss of time."

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* But see note in Chapter XVIII. on Scurvy, page 420.

Group "B," which includes pyrexia of uncertain origin, trench fever, myalgia and rheumatism, accounts for 26,024 admissions. Colonel Soltau considers that fully 20,000 of these were really trench fever, and, adding to this figure 1,500 of the cases of disordered action of the heart which is a frequent sequel of the fever, he ascribes 21,500 of his cases to trench fever, or, in other words, to infestation by lice.

From the two groups combined he concludes that 44 per cent. of the total admissions were due to diseases caused by dirt or lice and therefore preventible by sanitary measures.

Uncleanliness and verminous infection have consequently been brought into special prominence during the war as causes of sick wastage from this group of disease. In the South African War, diseases of the connective tissue and diseases of the skin together accounted for an admission rate of 46·83 out of the admission rate of 843·0 for all classes of sickness ; and, although these diseases may not in other areas and in other conditions rise to so large a proportion, yet they must in future be regarded as so powerful a cause of inefficiency that great efforts to prevent them are not only justifiable but necessary.

During the war four conditions, one hitherto undescribed by military surgeons and the other three barely mentioned, attracted much attention in France. Trench foot can be recognized in Larrey's notes of the winter campaign in East Prussia in 1806, and nephritis occurred to a considerable extent among the troops in the American Civil War, but trench fever is a form of disease which has escaped notice until now, and though gas gangrene had been occasionally seen in civil practice there is, according to Sir Anthony Bowlby, hardly any description of it in military surgery. Upon all these a great deal of original and experimental work was expended, and if in nephritis no great advance has been made towards its prevention or cure, much has been gained in the other three cases. Trench foot was at once studied with the greatest care. Many experiments were made in various forms of boots and leggings, and eventually by the use of long loose thigh boots, by the strict application of prophylactic treatment to preserve proper circulation, and by improvements in the trenches, its incidence was greatly reduced. It still, however, in 1917 accounted for 3,294 of Colonel Soltau's admissions. Trench fever is an excellent instance of the practical value of research to an army in the field. It was recognized in 1915 and proved to be infective by inoculation of volunteers early in 1916. Had that method been pursued at the time, the pathology of the disease and the means by which it was spread would soon have been discovered, but the use of volunteers for the needful experiments at the time was not permitted, and accordingly these discoveries were postponed till 1917-1918, when, with the help of 60 or 70 volunteers, the American pathologists settled the question in three months. The delay probably meant that about 200,000 cases might have been prevented had the experiments taken place earlier. Another striking instance may be drawn from the surgical triumphs which immediately followed upon the knowledge gained in the pathological laboratories regarding the anaerobic infections which produced gas gangrene.

What, then, are the lessons which may be learnt from such figures, imperfect though they are, and how can the experience of the war teach us to lessen sickness and consequent wastage in future campaigns?

In the first place, while the standard of sanitary discipline was excellent in such matters as water supply and disposal of excreta, the immense effect of uncleanliness in the production of disease must be recognized in future far more than it has been hitherto. Men are often crowded in dugouts and cellars, can only change their clothes or bathe at rare intervals, and are continually feeding in conditions which must convey infection if there is any infection to convey. The result is a sick rate from dirt diseases which amounts to nearly 50 per cent. of the total sickness in an army. That is sufficient to warrant the greatest possible effort to provide more baths, more laundries, more vermin destroyers, and to see that the men have opportunities of using them. Although measures to exterminate lice were energetically pursued from an early stage in the war, and the means of disinfestation constantly increased, it was not until the trench fever committee reported that the infection was carried by lice that the sanitary branch obtained the full equipment and facilities of which it had long been desirous.

Secondly, the war has shown the immense services which original research can render to preserve the efficiency of an army. The examples of trench fever, of cerebro-spinal fever, of gas poisoning, and of gas gangrene showed what wonderful results could be obtained by the union of clinical and pathological research not only at home, but also in the actual area of military operations. The mobile bacteriological laboratories were designed chiefly as aids to diagnosis and special treatment, but they went far beyond these limits and played a large part in the fresh discoveries of medicine and surgery. It cannot be doubted that in the future a prophylactic against dysentery will be discovered, and it can only be discovered by scientific experiment ; it is even possible that by the same method we may improve our means of preventing malaria.

Thirdly, the facts prove that in planning campaigns, especially in regions little known, the general staff should take the wastage by sickness into account as much as the wastage by wounds, and that not only should the army medical authorities be consulted concerning the probable loss from sickness and the consequent need for reinforcements, but their opinion should also be required concerning the best methods of prevention, including such local questions as sites for camps, destruction of insect carriers of disease, and purification of water, and also the wider and more general subjects of the provision of proper dietary, clothing and equipment. The medical side of the planning of a campaign is just as necessary for efficiency as the military, and the neglect of it must inevitably lead to an enormous amount of preventible wastage.

Lastly comes the great lesson of the war with regard to disease that, while to an army medical officer the fullest knowledge of all that tends to prevent disease is of the utmost importance, the treatment of patients admitted to hospital for injuries or disease, in other words, the clinical medicine and surgery of war time, is not of necessity rough in method or imperfect in attainment, but is susceptible of a high and exquisite perfection and affords scope for the finest scientific work.

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CHAPTER II.

ENTERIC GROUP OF FEVERS.

THE enteric group of fevers includes typhoid fever, due to infection with *Bacillus typhosus* of Eberth, and the paratyphoid fevers, due to infection with either *Bacillus paratyphosus A* or *Bacillus paratyphosus B*. The paratyphoid section may have to be enlarged to include at least one other variety, *Bacillus paratyphosus C*, which has strong claims to be considered as a definite and specific infection.

In the early months of the war there was confusion in the nomenclature of these diseases, owing to the lack of precision with which the term "enteric fever" was used by different medical officers; by some it was considered synonymous with typhoid fever, by others it was only considered to imply a group infection.*

It was not until March 1915 that official sanction was granted by General Headquarters in France for the use of the diagnosis "Enteric Group" on clinical grounds, with the obligation to change it later to typhoid, paratyphoid A or paratyphoid B when the precise nature of the infection had been determined in the laboratory.

A certain number of cases, in which, for various reasons, accurate bacteriological or serological diagnosis cannot be made, retain the diagnosis "Enteric Group." In describing this group of diseases, as they occurred during the war, the term enteric fever comprises the group infection considered as a whole. The terms typhoid and paratyphoid A or B indicate specific infections by their respective bacilli.

Enteric fever has long been recognized as likely to be more deadly to an army on active service than the bullets of the enemy, and the truth of this is shown in the statistics from previous campaigns.

In the South African War the British Army employed 557,653 men, with an average strength of 209,404, and there were 59,750 cases of enteric fever, with 8,227 deaths. This is equivalent to an admission rate of 285, with a death rate of 36 per thousand of average strength.

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* The nomenclature which army medical officers were required to follow was the official nomenclature of diseases drawn up by a joint committee appointed by the Royal College of Physicians. According to it enteric fever is a synonym for typhoid fever, and includes the sub-groups of paratyphoid A and B.

In the Spanish-American War the American Army employed 107,973 men and there were 20,738 cases of enteric fever, with 1,580 deaths. This is equivalent to an admission rate of 88·5 per thousand for the year 1898. Sternberg, in "Sanitary Lessons of the War," gives the annual death rate per thousand from typhoid fever at 14·8 in the American camps in Florida and Virginia during this war.

In the Franco-German War the Germans despatched 1,146,000 men across the frontier; these showed 73,393 cases of enteric fever, with 6,965 deaths.

In the French operations in Tunis, from a total strength of 20,000 men there were 4,200 cases of enteric fever, with 1,039 deaths.

In the Russo-Turkish War, the Russian Army of the Caucasus comprised 246,000 men and showed 24,475 cases of enteric fever, with 8,900 deaths.

No attempt was made in previous campaigns to differentiate typhoid from paratyphoid fevers, hence a considerable number of cases from which the foregoing statistics were compiled were probably paratyphoid. In view of the much lower mortality from paratyphoid fever it follows that the true percentage mortality of typhoid cases in previous wars has been higher than has been stated above.

With regard to the incidence of enteric fevers in 1914–1918, the official figures for the British Armies offer a welcome contrast to the experiences of previous campaigns.

The incidence of the enteric fevers in the expeditionary forces in the various theatres of war is shown in the following table:—

TABLE I.

Theatre of War.	Year.	Number of Cases.	Incidence per 1,000 of Ration Strength.	Number of Deaths.	Death Rate per 1,000 of Ration Strength.	Total Case Mortality per cent.	Mean Ration Strength of Force.
France ..	1914 (Aug.-Dec.)	388	—	47	—	12·1	—
	1915	2,351	4·0	130	·22	5·5	588,000
	1916	2,668	2·0	30	·02	1·12	1,274,200
	1917	1,166	·61	33	·012	2·8	1,884,100
	1918	334	·12	20	·007	5·9	2,528,400
E. Africa ..	1917	102	5·0	27	1·3	26·4	20,600 (approx.)
	1918	116	7·8	33	2·2	28·4	14,700 (approx.)
Salonika ..	1916	1,105	11·79	40	·42	3·62	93,684
	1917	529	2·61	19	·09	3·78	202,260
	1918	135	·84	6	·03	4·44	159,947
Italy ..	1918	141	1·5	15	·15	10·6	94,000
Egypt (excluding officers and Indian troops)	1916	2,950	17·35	66	·32	2·2	170,000
	1917	505	2·82	22	·12	4·3	179,000
	1918	401	1·87	51	·23	12·7	213,000

TABLE I.—*cont:*

Theatre of War.	Year.	Number of Cases.	Incidence per 1,000 of Ration Strength.	Number of Deaths.	Death Rate per 1,000 of Ration Strength.	Total Case Mortality per cent.	Mean Ration Strength of Force.
Mesopotamia	1916 (22 weeks only)	1,266	—	110	—	8·6	—
	1917	1,211	14·4	91	1·08	7·5	84,000 (approx.)
	1918	640	6·0	70	·55	10·9	106,000 (approx.)
Gallipoli ..	1915	4,241	—	uncertain	—	9·0 (approx.)	Not available.

No attempt has been made in the above table to differentiate between typhoid and paratyphoid fevers, and the totals do not represent all the cases of enteric fever that occurred in the British forces throughout the war, since cases occurring in Indian troops and native labour corps are not included, but it is believed that the figures are as accurate as can be determined at present for the periods and theatres of war concerned.

The total number of cases and deaths in this table shows that in upwards of four years and in six theatres of war, with an average mean ration strength of nearly two million troops, there were only 20,149 cases of typhoid and paratyphoid fever with 1,191 deaths, giving a total case mortality of 5·4 per cent.

The relative incidence of the three infections in the various theatres of war, as far as it was possible to identify them with certainty, is shown in the following tables :—

TABLE II.

Incidence of the Enteric Group of Diseases.

Theatre of War.	Year.	Number of Cases.				Incidence per 1,000 of Ration Strength.			
		Typh.	Para. A	Para. B	Enteric Group	Typh.	Para. A	Para. B	Enteric Group
France ..	1914	253	5	31	99	—	—	—	—
	1915	805	281	1,043	222	1·3	·47	1.7	·3
	1916	729	580	1,009	350	·57	·45	·7	·27
	1917	227	173	471	295	·12	·08	·24	·15
	1918	90	43	156	45	·03	·015	·06	·015
Salonika ..	1916	97	212	203	593	1·03	2·26	2·16	6·32
	1917	81	136	92	220	·40	·67	·45	1·08
	1918	30	47	20	38	·18	·29	·12	·23
Italy ..	1918	33	23	61	22	·35	·25	·6	·26
Egypt ..	1916	99	187	143	2,521	·58	1·1	·84	14·83
	1917	13	70	74	348	·07	·38	·41	1·94
	1918	31	66	46	258	·14	·3	·21	1·2

TABLE III.

Incidence of Enteric Group of Diseases in Mesopotamia and Gallipoli.

Theatre of War.	Year.	Typh.	Para. A	Para. B	Enteric Group.	Proved Cases.
Mesopotamia	July–Dec. 1916	12·3%	74·4%	13·2%	1,018	446
(quoted from Ledingham)	Jan.–June 1917	8·9%	77·2%	13·8%	239	101
	July–Dec. 1917	21·3%	72·5%	6·0%	544	197
	Jan.–June 1918	36·6%	50·4%	12·8%	170	101
	July–Dec. 1918	37·7%	47·2%	14·9%	209	127
Gallipoli .. (Based on a report by Martin and Upjohn)	1915	7·0%	61·0%	32·0%	—	—

The information afforded by these tables is not of equal value in all the theatres of war. The chief difficulty lies in the widely different proportion of cases which remain classified "enteric group."

Considering the great difficulties under which all bacteriological work laboured throughout the eastern campaigns, it is inevitable that the proportion of "group" to proved cases should be particularly high in these areas, while the figures for France are the most reliable owing to the low proportion of these undiagnosed cases.

It is nevertheless reasonably certain that the above tables represent with fair accuracy the relative incidence of typhoid and the two paratyphoid fevers.

It will be seen that only in France was typhoid fever responsible for as many as one half the total cases and that in the other campaigns the proportion was usually less than one quarter; but that whereas in France and Italy paratyphoid B was about three times as frequent as paratyphoid A, in Salonika paratyphoid A was more frequent than paratyphoid B in the proportion of 32 to 27; in Egypt the proportion of paratyphoid A to paratyphoid B was as 9 to 7, while in Mesopotamia paratyphoid A was five times as frequent as paratyphoid B and three times as frequent as typhoid until 1918, when there was a notable increase in typhoid and diminution in paratyphoid A.

It would not be fair to assume that the relative proportions of the three infections shown above obtained in previous campaigns because there can be no doubt that, taken as a whole, prophylactic inoculation has conferred a greater mass immunity against typhoid fever than against either of the paratyphoids. This must be so if only because triple vaccine was not introduced in any theatre of war until January 1916 and cannot have become efficiently established until the end of that year.

At the outbreak of war typhoid fever was endemic in every theatre. Paratyphoid B was very rare in England, but it was fairly common on the continent, especially in Flanders, Alsace, parts of Middle Europe and Macedonia, while paratyphoid A was practically unknown except in India, Africa, Asia Minor, Turkey and possibly a few seaport towns like Marseilles, where there is a constant interchange between Europe and Africa.

The natural sequence of events as regards the British forces in France would be that typhoid should develop within the first few weeks or months, accompanied or closely followed by paratyphoid B, both acquired locally from water or carriers, but that the advent of paratyphoid A should be delayed until contact had been established by our troops from England with men who had served in India or the East, or alternatively with French troops who had served in Africa or been associated with French colonial forces. This is precisely what occurred; cases of typhoid fever developed in the latter part of September 1914, and were attracting serious attention by the second week in November, but it was not until December 5th that an undoubted case of paratyphoid B was detected, and the first proved case of paratyphoid A was admitted to hospital on December 14th; further, it is noteworthy that the early cases of paratyphoid A were all in troops who had either come to France from India or who had been in close contact with such troops.

The steady relative increase in the number of paratyphoid cases in France, especially paratyphoid B—for paratyphoid A was always numerically insignificant—as well as the steady decline in all forms of enteric fever in the last quarter of 1915 is shown in Table IV, compiled from the admission and discharge books of No. 14 Stationary Hospital, which dealt with more than half the total number of cases from the entire force during the period under review. This table also shews that with properly organized laboratory work the proportion of cases in which final diagnosis is impossible is relatively small; the percentage of cases under the heading "enteric group"

TABLE IV.

Monthly admissions November 1914—*December* 1915 *at No.* 14 *Stationary Hospital, France.*

Month.	Year.	Total Cases.	E. Group.	Typh.	Para. A	Para. B	Mixed Infections.	Total Deaths	Deaths from			Total Case Mortality. per cent.	Percentage Mortality.		
									Typh.	Para. A	Para. B		Typh.	Para. A	Para. B
November ..	1914	31	31	—	—	—	—	3	—	—	—	9·7	—	—	—
December ..	1914	140	35	87	4	14	—	20	20	—	—	14·28	17·0	—	—
January ..	1915	148	45	63	9	31	—	16	15	—	1	10·8	16·6	—	2·2
February ..	1915	141	27	46	21	47	—	10	7	1	2	7·0	12·3	3·9	3·5
March ..	1915	162	30	67	21	44	—	21	19	—	2	12·9	23·0	—	3·8
April	1915	103	22	49	7	25	—	11	8	—	3	10·6	12·9	—	9·3
May	1915	106	13	41	7	45	—	11	8	—	3	10·3	17·0	—	5·8
June	1915	127	5	34	16	72	—	4	2	—	2	3·1	5·5	—	2·2
July	1915	128	5	26	15	78	4	4	2	—	2	3·1	7·4	—	2·4
August ..	1915	74	1	24	9	38	2	1	—	—	1	1·3	—	—	2·6
September ..	1915	118	4	41	16	55	2	—	—	—	—	—	—	—	—
October ..	1915	57	3	15	6	31	2	—	—	—	—	—	—	—	—
November ..	1915	50	8	9	8	25	—	—	—	—	—	—	—	—	—
December ..	1915	40	4	14	8	17	6	—	—	—	—	—	—	—	—

drops steadily as the efficiency of the laboratory workers and the co-ordination between clinician and bacteriologist increase.

At the same time there will always be a small residuum, up to 5 per cent., in which the clinical picture is that of enteric fever but the bacteriological and serological findings do not support the diagnosis. This difficulty was apparent in 1915 and was increased considerably in later years by the adoption of triple inoculation; the question will be considered again when the diagnosis of the enteric group is under discussion.

Just as paratyphoid A was conveyed to the western front from India and Africa, so was paratyphoid B conveyed to Mesopotamia by the divisions which proceeded thither from Europe and Egypt in 1916. Prior to the arrival of these troops the Mesopotamia force was composed exclusively of troops from India where, as in Mesopotamia, paratyphoid B was practically unknown; so that enteric fever was restricted in 1915 and the early part of 1916 to typhoid and paratyphoid A. Boney, Crossman and Boulenger state that paratyphoid B was not diagnosed till March 1916, which coincides with the arrival of a British division from Gallipoli and Egypt. These authors find from an analysis of 650 cases after this date that the proportions were: typhoid 21 per cent., paratyphoid A 65 per cent., paratyphoid B 14 per cent., so that paratyphoid B obtained a firm foothold when once it had been introduced; indeed, for 1918 the incidence per thousand of paratyphoid B, including Indian troops, is nearly twice that for 1917.

Figures dealing with the incidence of the enteric group in the Gallipoli expedition are not very reliable, owing to the nature of the campaign and the extreme difficulty of evacuating the sick, as well as the long distances between the fighting zone and the hospital bases. Coutts gives clinical notes of 66 cases of paratyphoid B and 63 cases of paratyphoid A; Martin and Upjohn found paratyphoid A to be nearly twice as frequent as paratyphoid B. It is noteworthy, in connection with this campaign, to find that a considerable number of cases evacuated as dysentery were ultimately proved to be suffering also from paratyphoid fever, especially paratyphoid B.

In Salonika, paratyphoid A was more frequent than either paratyphoid B or typhoid; and paratyphoid B was more numerous than typhoid till 1918, when it became the least common of the three.

In Italy, in 1918, the relative proportions resembled those obtaining in France, except that paratyphoid A was rather higher; the actual incidence of enteric fever per 1,000 of ration strength was, however, more than ten times as high.

In Egypt the very large proportion of group cases in 1916 makes comparison difficult, but it appears that paratyphoid A was numerically preponderant, both paratyphoid A and paratyphoid B being higher than typhoid. In 1917 typhoid was seven times less common than either paratyphoid A or paratyphoid B but paratyphoid B was fractionally higher than paratyphoid A; in 1918 typhoid was still the least numerous, but paratyphoid A was definitely higher than paratyphoid B.

Mortality.

The total case mortality per cent. for the three varieties of enteric fever grouped together can be determined fairly accurately, and, as has been shown in Table I, it varies considerably with the different campaigns but may be summarised as follows:

TABLE V.

Summary of case mortality from the enteric fevers in different theatres of war.

France	3·8 per cent.
Salonika	3·9 ,,
Egypt	6·4 ,,
Mesopotamia	8·7 ,,
Italy	10·6 ,,
East Africa	27·4 ,,

The high death rate in East Africa may be explained by the extreme rigour of that campaign and the necessity for operating at a great distance from a properly equipped base in a very unhealthy climate. It is also probable that many mild cases of group infection were overlooked, and it is certain that many of the deaths were due rather to the presence of a coincident infection, such as malaria or relapsing fever, than to the enteric infections.

There is one point of special interest in the mortality columns in Table I., namely, the fact that the low water mark of percentage case mortality was reached in 1916 and that a notable increase occurred in both 1917 and 1918. This increase was more or less apparent in every theatre of war where reliable figures are available, as follows:—

TABLE VI.

Showing increase in case mortality after 1916.

	1916.	1917.	1918.
France	1·12%	2·8%	5·9%
Salonika	3·62%	3·78%	4·44%
Egypt	2·2%	4·3%	12·7%
Mesopotamia	10·9%	7·5%	10·9%
East Africa	—	26·4%	28·4%

It is necessary to enquire briefly into the possible reasons for this increase in case mortality. It will be remarked that the increase dates from the adoption of triple vaccine, so that it might be thought that triple vaccine to some extent decreases the immunity conferred against typhoid fever. If this were so, one would expect to see a definite increase in the case mortality from typhoid in protected men, and also to find that the increase is chiefly in typhoid as opposed to paratyphoid cases. The increase in typhoid mortality is as follows :—

TABLE VII.

Case mortality from proved cases of typhoid.
(Western Front.)

	Protected by Inoculation.	Unprotected by Inoculation.
1915	7·54%	23·2%
1916	1·58%	8·3%
1917	7·73%	12·12%
1918	13·84%	24·0%

A similar increase is thus shown in the figures for those who are unprotected, and it is obvious that there must be some other factor at work to explain the drop to 8·3 per cent. in the unprotected in 1916 with the subsequent rise to 24 per cent. in 1918. The difficulty of getting satisfactory re-inoculation at the end of 1917 and throughout 1918 would tend to produce a higher death rate among the partly protected.

The points which seem to be of great importance in this connection are, first, the undoubted lowering of all powers of resistance to infection in the nation as a whole and in the troops in particular by four years of continuous warfare, and, secondly, the increased average age and lower physical categories of an army which became to all intents and purposes a nation under arms.

In attempting to arrive at the individual case mortality of the three enteric infections, there is the difficulty, already mentioned, of including the cases of the enteric group in which no final diagnosis has been possible. To ignore these cases might in some cases give unduly high results by eliminating a considerable number of cases with a low death rate. It is probable that a fairly correct result will be obtained by assuming that the enteric group cases are made up of typhoid, paratyphoid A, and paratyphoid B in like proportion to the proved cases for the same area during the same period of time, and that the infections causing death in group cases are relatively proportionate to those causing death in proved cases. This method gives the following results for France, Italy and Egypt :—

TABLE VIII.

Approximate percentage case mortality from typhoid, paratyphoid A and paratyphoid B.

Theatre of War.	Year.	Typhoid.	No. of Cases.	Para. A.	No. of Cases.	Para. B.	No. of Cases.
France ..	1914	13·5	340	—	7	4·9	41
	1915	12·0	889	·6	314	2·9	1,148
	1916	1·6	839	1·5	668	·7	1,161
	1917	6·5	304	·8	233	1·9	529
	1918	15·5	104	2·6	50	1·4	180
Italy ..	1918	22·3	39	3·7	28	6·4	72
Egypt ..	1916	3·7	659	2·03	1,287	1·6	1,004
	1917	Sufficient data not available as no deaths were recorded in proved cases of paratyphoid.					
	1918	37·0	87	6·3	179	7·8	135

The returns from Salonika and Mesopotamia do not permit of analysis on these lines.

For purposes of comparison the death rate from *proved cases* of the three infections is shown in the following table :—

TABLE IX.

Percentage case mortality from proved cases of typhoid and paratyphoid.

Theatre of War.	Year.	Typhoid.	No. of Cases.	Para. A.	No. of Cases.	Para. B.	No. of Cases.
France ..	1915	13·0	805	·71	281	1·91	1,043
	1916	1·9	729	1·7	580	·7	1,009
	1917	8·3	227	·56	173	2·1	471
	1918	16·5	90	2·3	43	·6	156
Italy ..	1918	24·2	33	4·2	23	6·5	61
Egypt ..	1916	6·06	99	3·2	187	2·08	143
	1917	23·0	13	—	70	—	74
	1918	41·0	31	6·06	66	8·6	46
Mesopotamia	1916 1917 1918	11·4	320	3·6	532	7·5	120

The value of the figures in the foregoing tables depends largely on the totals of the cases, for when there are few cases the value is slight; but it is evident that the case mortality from all the enteric infections varies within wide limits from time to time in the same theatre of war, and also varies directly with the efficacy of the general hygiene, transport, and medical arrangements.

The proverbial severity of these infections in hot climates is noticeable in the figures from Egypt and Mesopotamia. The theory held by many who had worked in India that paratyphoid A was practically negligible as a cause of death appears to be fallacious when applied to active service conditions in the East, for there was in 1918 a case mortality of over six per cent. from this disease in the Egyptian forces, and in France the death rate for the same year was more than two per cent. This high death rate in Egypt was in part explained by an outbreak of malignant tertian malaria which complicated the enteric infections.

The relative mortality from paratyphoid A and B appears to vary greatly with time and place, as shown in Table IX., but here again the totals are often too small to be reliable, and the only safe deduction seems to be that they are both very much less severe infections than typhoid under like conditions.

The total figures available at present for proved cases from France, Italy, Egypt and Mesopotamia give a mortality table approximately as follows :—

TABLE X.

Typhoid	9·8%	mortality	in 2,472	cases.
Paratyphoid A	2·6%	,,	,, 2,023	,,
Paratyphoid B	1·55%	,,	,, 3,160	,,
Total Paratyphoid	2·1%	,,	,, 5,183	,,

This is striking in one particular, namely, that the figure for paratyphoid A is considerably higher than that for paratyphoid B, a fact that is opposed to the general impression as gathered from the analyses of smaller series of cases made before the introduction of triple vaccine. Thus, in 1915, Torrens and Whittington found the mortality to be four per cent. for paratyphoid B, and less than one per cent. for paratyphoid A, while Boidin in January 1916 reported a series of cases in the French Army with a mortality of six per cent. for paratyphoid B and 1·4 per cent. for paratyphoid A. Rathery in a large series of cases of paratyphoid B found a mortality of over six per cent.

A possible explanation of this difference in the mortality of the two infections is that the vaccine used from 1916-1918 conferred more protection against paratyphoid B than against paratyphoid A, a suggestion that is to some extent supported by the low titre to paratyphoid A, so often shown after triple inoculation; or again the severity and frequency of paratyphoid A in tropical and sub-tropical climates may more than counterbalance the greater relative severity of paratyphoid B on the Western Front. Hence it may well be that in a civilian uninoculated population in Western Europe, an epidemic of paratyphoid B would be found to be attended with a higher death rate than would one of paratyphoid A, with a figure for either disease of from three to five per cent.

Ætiology.

With regard to the various factors affecting the ætiology of these diseases there is no reason to suppose that any which may be said to predispose to typhoid fever predispose also in any greater or less degree to either of the paratyphoid infections. The predisposing causes can be considered under two headings; first, those of *environment*, which influence the presence and distribution of the infective material, and secondly, those of *immunity*, which influence the individual's capacity to neutralize a given dose of infective material.

Although a tropical or sub-tropical climate does not favour the growth of the bacilli of enteric fever outside the body, it nevertheless favours their distribution by flies and in dust, while the defective sanitary arrangements amongst the inhabitants of the East and Near East make enteric fever widely endemic in these regions. Before the war typhoid and paratyphoid A were very prevalent throughout the East, while paratyphoid B was practically unknown, so that in a sense it might be said that a tropical climate predisposes to typhoid and paratyphoid A rather than to paratyphoid B, and conversely that a cold or temperate climate predisposes to paratyphoid B rather than to paratyphoid A. Whether paratyphoid B will speedily die out in the East and paratyphoid A in the West, now that their respective sites of election have been enlarged, remains to be seen. Although epidemics may start at any time of the year, the summer and autumn are always likely to show the greatest number of cases and also the most severe ones. The effect of the external temperature is undoubted. Enteric fever is more frequent and more severe along the Mediterranean littoral than in the more northern parts of Europe; for the same reason the disease persists in a serious form in Egypt, India, Central America, and the Philippines.

The number of bacilli present in subsoil water increases with the utmost rapidity as soon as men are occupying the surface of the soil. Vincent gives the following analysis from a camp in which typhoid was constantly occurring. Before the arrival of the troops the water was very pure and contained only 100 ordinary bacteria per c.c. Six days later there were 770 bacteria, forty days later 6,960, sixty days later 14,900, and three months afterwards 38,000 per c.c.

In highly cultivated districts there is a great likelihood of the subsoil water becoming infected as a result of the practice of manuring the earth with human excrement. It is true that the typhoid bacillus does not survive in drinking water more than three to five days, but under suitable conditions the water is constantly being re-infected with fresh relays of virulent bacilli from a saturated soil. The importance of drinking water as a cause of enteric fever has been proved in numerous epidemics, and in war time in the field all drinking water should therefore be sterilized efficiently before use.

It has been shown that flies can carry typhoid and other pathological bacilli in their stomachs, on their feet, and on their probosces. Although the curve of enteric fever does not follow closely that of the fly pest, and the extent to which flies may be responsible for the spread of enteric fever is not fully established, these insects and the fingers of the " carrier " may, however, be regarded as playing the leading parts in causing the dissemination of typhoid infected material in war time. The specific bacilli are always likely to be present owing to the existence of some recent case in the neighbourhood or to the presence of a " carrier " among the population. A man sickening for enteric fever may be infectious for three or four weeks before he realizes he is ill. A " carrier " may convey infection for months or years after he has recovered from the disease and the bacilli may live in fæces or urine under favourable conditions of moisture for 100 days, and for upwards of 40 days in the absence of moisture.

Hence the most important factors predisposing to the occurrence of enteric fever in war are the manifest impossibility of securing an absolutely perfect disposal of all fæcal and urinary matter and the difficulty of excluding all " carriers " from an army. It has been shown experimentally that a large percentage of men soil their fingers both during micturition and defæcation, especially the former ; and the contamination of food or water is more than likely to result.

Fletcher investigated bacteriologically one thousand men who were convalescent from enteric fever ; he found that prophylactic inoculation diminished the frequency of " carrier " development amongst infected men but did not abolish it, and that 0·6 per cent. of all convalescent male enteric cases are " carriers." Small epidemics have, in peace time, frequently been traced to cooks, waiters and others, who were "carriers," and the same source of infection has been proved repeatedly during the war to explain a sudden crop of cases in the same unit when neighbouring units have been relatively or absolutely free.

With regard to individual immunity, there are numerous personal factors upon which immunity from enteric fever seems to depend. A previous attack confers a very great though not absolute immunity from re-infection with the same bacillus. It is estimated by Vincent and Muratet that not more than two per cent. of persons who have had typhoid fever can contract it a second time. But there is no experimental evidence that typhoid fever confers any immunity from paratyphoid fever or *vice versa*.

Prophylactic inoculation with triple vaccine confers relatively great immunity against typhoid and both forms of paratyphoid fever, the degree of immunity increasing up to a point with the number of injections employed.

Real immunity is only relative, but it appears that the Japanese and Chinese are not so susceptible as Europeans. Enteric fever, for example, has been stated to be less frequent in the Japanese than in the Russian Army in the Russo-Japanese War, and there was a similar experience in the Chinese expedition of 1901. The Hindu races appear to suffer but slightly from enteric fever in spite of their primitive hygienic and sanitary arrangements. It is held by some that the immunity of the Eastern races is apparent rather than real, as it is thought that the bulk of the population gets infected in childhood. This apparent relative immunity from enteric fever amongst the Asiatic races is borne out by the figures from our forces operating in Egypt and Mesopotamia.

TABLE XI.

Showing relative incidence in British and Indian Races.

	Incidence per 1,000 of Ration Strength.		Case mortality per cent.	
	British.	*Indian.*	*British.*	*Indian.*
Egypt :—				
1916	17·35	1·15	2·2	—
1917	2·8	·9	4·3	7·6
1918	1·87	·5	10·4	9·5
Mesopotamia :— ..				
1917	2·5	·4	10·8	22·3
1918	2·5	·8	6·4	18·3

The Indian figures for Mesopotamia, however, include a large number of followers, of whom only 20 per cent. were protected by inoculation in 1917 and 50 per cent. in 1918. Of the Indian troops proper about 80 per cent. were protected in 1918 and 50 per cent. in 1917, and of the British troops 75 per cent. in each year. If we exclude the Indian followers, in order to obtain a better standard for comparison with British troops, we find that the mortality for Indians in 1917 was 22 per cent. and in 1918 12·8 per cent., with an incidence of 0·3 and 0·5 per 1,000 respectively. It thus appears that in the Indian races there is a real insusceptibility to acquiring enteric fever, but that there is a tendency for the infection when acquired to be exceptionally severe.

On the other hand, the high death rate in Indian troops can to some extent be discounted by the probability that many mild cases were never reported as enteric fever, but were allowed to run their course as pyrexia of uncertain origin.

If this apparent racial insusceptibility is due principally to immunity acquired as the result of disease in childhood, it would be expected that the incidence of paratyphoid B in Indian troops would be more nearly that obtaining in the British troops, at any rate in 1918 when the paratyphoid B infection, which was at first confined to the British troops who brought it with them to the country, had become more widely disseminated. This view is supported to some extent by the official figures for 1917 and 1918, dealing only with men unprotected by triple vaccine.

TABLE XII.

	British.		*Indian.*
Incidence of Paratyphoid B per 1,000 of ration strength in unprotected men	1917	3·92	·02 (one case only)
	1918	·64	·4

The conclusion that enteric fever has run a graver course when it has attacked the Indian troops than when it has attacked the British is upheld by Ledingham, who published the following figures from Mesopotamia for 1916–17–18.

TABLE XIII.

Case Mortality in British and Indian Troops.

	British.	*Indian.*
Typhoid	11·4 per cent.	27·2 per cent.
Paratyphoid A	3·6 ,,	11·3 ,,
Paratyphoid B	7·5 ,,	16·6 ,,
Enteric Group	10·0 ,,	20·7 ,,
Enteric Fever as a whole ..	8·7 ,,	20·5 ,,

Age is recognized as playing an important part in the susceptibility to the enteric infections. No age is immune, but 46·5 per cent. of all cases occur between the ages of fifteen and twenty-five years. The statistics of the city of Paris for thirty years show that men are most frequently attacked between the ages of twenty and twenty-four years, while the liability to infection remains high up to thirty years of age. Further, between the ages of twenty and twenty-five, the death rate is nearly twice as high in men as in women, 67·1 per cent. to 37·6 per cent. An army is therefore composed largely of those members of the community who are most liable to become infected with enteric fever in a severe form.

There are three other personal factors of great importance as predisposing in wartime both to a high incidence of, and to a heavy death-rate from enteric fever; they are physical fatigue, mental strain, and the necessity for a more or less prolonged journey after the infection has begun to show its symptoms. No one who has worked amongst enteric fever patients can have failed to notice that those cases are most severe which have been longest delayed in transit to the enteric fever hospital.

As regards the *exciting causes* in the ætiology of enteric fever, the disease as at present understood includes infection by one of three specific micro-organisms and thus comprises three distinct though very similar diseases, namely :—

Typhoid Fever due to infection by *Bacillus typhosus.*

Paratyphoid A Fever due to infection by *Bacillus paratyphosus A.*

Paratyphoid B Fever due to infection by *Bacillus paratyphosus B.*

The specificity of these three micro-organisms has been proved beyond doubt by biochemical and serological tests. *Bacillus typhosus* was identified by Eberth in 1880–81, but it was not until 1896 that Achard and Bensaude gave the first account of a bacillus other than *Bacillus typhosus* recovered from the urine of a case of apparent enteric fever. This organism is now recognized as being *Bacillus paratyphosus B.* In 1898 Gwyn recorded a similar experience; in his case the bacillus was recovered from the blood stream. In 1900 Cushing described an organism not *Bacillus typhosus,* which he recovered from the pus of a chondro-costal abscess following an attack of apparent enteric fever. In 1900 and 1901 Schottmüller described organisms which biochemically were intermediate between *Bacillus typhosus* and *Bacillus coli* and which did not agglutinate with typhoid serum. In 1902 Buxton split the paratyphoid organisms into two groups A and B, A being closely allied to *Bacillus typhosus* and B to paracolon. In 1904 Firth described fully paratyphoid A as it occurred in British troops in India, work which was later amplified by Harvey, Grattan, Wood and other officers of the Royal Army Medical Corps.

In 1904 Bainbridge in the Milroy lectures differentiated clearly between the paratyphoid bacilli A and B on the one hand, and the organisms of food poisoning, *Bacillus suipestifer,* isolated in 1885 by Salmon and Theobald Smith, and *Bacillus enteritidis* on the other. A third member of the food poisoning group *Bacillus aertrycke* was first described in 1898 by Durham and de Nobele, working independently ; this organism, though closely allied to *Bacillus paratyphosus B,* is nevertheless specifically distinct, as is shown by Perry and Tidy in their report on an epidemic of this nature published in 1918. Most bacteriologists now hold the view that *Bacillus suipestifer* and *Bacillus aertrycke* are identical.

Although we can thus dissociate completely from enteric fever a considerable group of infections by allied bacilli, there is nevertheless a distinct possibility that the legitimate paratyphoid group is not absolutely restricted to the two members A and B. Apart from blood infection with members of the food-poisoning group of organisms which, clinically, do not as a rule very closely resemble paratyphoid fever, there is a rare class of case which clinically is enteric fever but in which the agglutination curve of the patient's serum offers no corroboration of the diagnosis. Occasionally in such cases a bacillus will be recovered from the blood, urine or fæces, which bacteriologically is not *Bacillus typhosus,* or *paratyphosus A* or *B* on the one hand, or a member of the food poisoning group on the other. This bacillus, however, agglutinates with the patient's own blood serum and is therefore almost certainly responsible for the infection concerned. Such bacilli are commonly reported by the bacteriologist to be culturally indistinguishable from *Bacillus paratyphosus B.* It is reasonable to regard such cases as being a variety of paratyphoid fever as yet unclassified. This view is corroborated by the experience of Mackie and Bowen, and MacAdam in Mesopotamia ; these workers, independently, while investigating cases of clinical enteric, isolated from a series of cases a bacillus culturally indistinguishable from *Bacillus paratyphosus B* which proved by agglutination and absorption tests to be an additional member of this series. A specific high titre serum was successfully prepared for this bacillus by Mackie and Bowen for the purpose of diagnosing other cases of the same infection. Ledingham regards this bacillus as an Eastern variant of *Bacillus paratyphosus B* but, in view of its persistent inagglutinability to ordinary paratyphoid B serum, it seems that the name *Bacillus paratyphosus C*, as suggested by Hirschfeld, would be justifiable. Ledingham states that he has lately received a strain of this organism from East Africa.

Similar cases have been reported from Macedonia, where Willcox found that 10 per cent. of the cases of clinical enteric were due to a non-agglutinable *Bacillus paratyphosus B*.

Archibald describes eight cases in Sudanese soldiers clinically resembling enteric fever, but proved by blood cultures to be due to organisms unidentified but definitely not typhoid or paratyphoid.

On the whole, it would be well to keep an open mind for the present on the question of the eventual enlargement of the true paratyphoid group of diseases.

Morbid Anatomy.

With regard to the morbid anatomy of the disease, the post-mortem appearances in cases of typhoid fever are too familiar to need description here, and all the lesions ordinarily described have found a place in the records of the fatal cases of the war. A great diversity of possible lesions is naturally to be expected in a disease like typhoid fever, which is essentially a bacillæmia at the time of onset of symptoms and often for the first two or three weeks of its course, as well as during part of any relapses that may occur. Further the bacilli do not leave the system when they cease to be present in the blood stream, for in fatal cases they are always to be recovered after death from the gall bladder, nearly always from the spleen and bone marrow, usually from the mesenteric glands and frequently from the kidneys, the fauces, and the lungs if pneumonia has been a feature of the case.

The persistence of the bacilli in the body tissues is shown by the percentage of cases—about 2 per cent. in uninoculated persons—who remain either fæcal or urinary carriers for months or years, and also by the fact that sub-periosteal and other abscesses occurring late in convalescence can often be shown to contain the specific organism.

Though fatal cases of typhoid as a rule show very marked intestinal lesions, yet the extent or severity of the ulceration in the intestines is not necessarily an indication of the severity of the disease from the point of view of general systemic intoxication. The following case illustrates this point :—

Rfm. H., age 22. (Not protected by inoculation.)—Admitted on tenth day of disease with a positive diagnosis of typhoid fever by blood culture. Clinically a very severe typhoid fever of toxic type, the rapidity of respirations being due to toxæmia rather than any local pulmonary condition. There was a plentiful crop of spots and moderate enlargement of the spleen, also a tendency to diarrhœa till the sixteenth day. The rate and character of the pulse indicated an unfavourable issue. The patient remained semi-conscious and delirious from the time of admission until he died seventeen days later on the twenty-seventh day of illness. The agglutination reaction to *Bacillus typhosus* was negative on the tenth day, positive on the fifteenth day and weakly positive on the eighteenth day.

At the *post-mortem* examination there was no trace of any ulceration of the intestines, nor were the mesenteric glands soft or swollen with the chocolate discoloration usual in typhoid fever. The liver was pale, soft and rather larger than normal, the spleen weighed 8 oz. and was soft and diffluent. The lungs showed capillary bronchitis at the bases. The heart was dilated and the myocardium showed fatty change. There was a row of recent soft, fleshy vegetations along the three aortic cusps indicating commencing ulcerative endocarditis; *Bacillus typhosus* was recovered from the bile after death, but not from smears of the cardiac vegetations.

It is relatively rare for ulceration to be practically restricted to the large intestine in typhoid fever, though far from unusual in paratyphoid B.

The following notes illustrate such a case :—

Gr. C., age 22. (Inoculated January 13th and January 23rd 1915.)—Taken ill January 23rd, 1915. Admitted to hospital on sixteenth day of illness. Clinically a severe toxic case presenting no special features until the thirty-first day when there was a smart hæmorrhage; there was a smaller hæmorrhage the next morning and a large one the same evening from which the patient never rallied. The bowels had been opened freely throughout the illness but there was no profuse diarrhœa at any time, nor was there tenesmus.

Post-mortem there were only six healing ulcers in the lower part of ileum; the whole of the large gut from cæcum to sigmoid, and especially the latter, was crowded with large ragged unhealthy looking ulcers, the general appearance being somewhat reminiscent of dysentery. *Bacillus typhosus* was cultivated from the gall bladder and from the spleen; no bacteriological evidence of dysentery was obtained, in spite of a most thorough investigation.

Prior to the war but little was known as to the differences, if any, in the morbid anatomy of the paratyphoid fevers as contrasted with typhoid. It has now been established that there is no essential difference; any lesion that may be met with in typhoid may be encountered in either of the paratyphoids.

Since the gross mortality of paratyphoid is probably less than one quarter that of typhoid, it is obvious that the average lesion will be less intense in the former, but since only the very severe infections prove fatal it is natural that the post-mortem findings should approximate closely to those of typhoid. As a matter of practical experience they are indistinguishable. Dawson and Whittington, in an analysis of fourteen fatal cases of paratyphoid B and two of paratyphoid A summarized the cause of death as follows :—

Perforation	2 cases.
Peritonitis from infected appendix	2 cases.
Hæmorrhage	2 cases.
Hæmorrhage and toxæmia ..	3 cases.
Toxæmia	4 cases.
Pneumonia	2 cases.
Splenic abscess	1 case.

The same writers also noted the tendency for paratyphoid B to affect the large intestine as well as, or to the exclusion of, the ileum ; thus in two of their cases the large intestine alone was involved, in seven both small and large gut were affected, in four the small intestine only was concerned. In three cases of this series, two paratyphoid B and one paratyphoid A, the appendix was acutely inflamed and had determined the incidence of peritonitis ; in two cases, one paratyphoid B, one paratyphoid A, there was definite enteric ulceration in the appendix.

There is also a distinct tendency for metastatic pus formation in infections from *Bacillus paratyphosus B* ; thus in the fifteen cases mentioned above there were two spleen abscesses, two lung abscesses, one of which had caused a secondary empyema, and one abscess in the liver.

Since there are only two cases of paratyphoid A in this series, it is obvious that it is impossible to deduce very much as to the morbid anatomy of this disease. In a number of fatal cases of paratyphoid A, observed in Mesopotamia in 1916 by Torrens, the lesions were in the main identical with those of typhoid fever. Some predilection for the large intestine was noticeable, especially to the exclusion of the lymphoid tissue, but metastatic abscesses were not conspicuous. In some of the cases in which death occurred, rather from a complicating heat stroke than from the primary infection, the intestinal lesions were very trifling, sometimes amounting to no more than hyperæmia of Peyer's patches in the lower part of the ileum ; occasionally even this was wanting.

Carles discussing a series of 170 cases of paratyphoid in the French Army, with eight deaths, confirms the frequency of the involvement of the large intestine, as also the tendency for abscess formation ; he also observes that there may be no intestinal lesion present even in fatal cases. MacAdam records a fatal case of paratyphoid B complicated by thrombosis of the upper end of the left internal carotid artery extending upwards into the middle cerebral artery and the lenticulo-optic and lenticulo-striate branches. There was also thrombosis of the cortical branches of the right middle cerebral artery. No venous thrombosis could be made out in the brain or elsewhere, but the spleen showed two large hæmorrhagic infarcts in which purulent softening had commenced.

Scott and Johnson describe a small brain abscess in the right optic thalamus, found *post mortem* in a case which developed left hemiplegia during the course of paratyphoid B infection; unfortunately no attempt was made to recover *Bacillus paratyphosus B* from the abscess contents, so the possibility of a coincident infection cannot be absolutely excluded.

The great severity of the toxæmia as well as of the specific lesions in certain fatal cases of paratyphoid fever is shewn in a case of paratyphoid B published by Hichens and Boome. Clinically the patient presented all the features of advanced typhus fever including a maculo-petechial rash on the trunk. Death took place on the 14th day of the disease. *Post mortem* there was hæmorrhagic infarction in the lungs with early grey hepatisation at the right base. The entire intestine, large and small, showed acute inflammatory change but no ulceration. The mesentery was inflamed, the mesenteric glands swollen and hæmorrhagic, both kidneys were riddled with abscesses and the bladder showed acute purulent cystitis. The swollen spleen showed hæmorrhagic areas on section. This man had had antityphoid inoculation in 1915 and two doses of triple vaccine in June 1917, three months before the onset of his fatal illness.

Symptoms.

As regards the clinical features of typhoid fever as seen in unprotected men in war time, these do not show any material differences from the clinical features noted in the many classical descriptions of this infection. The average of such cases was severe, very much more so than the average case seen in civil hospitals in England during the ten years preceding the war. The mortality was far higher and the graver complications were more frequent than in the civilian cases. This severity of infection is explained by the age and environment of the fighting man, the fatigue and hardship he is undergoing at the time of infection and the inevitable delay before he reaches the infectious diseases hospital.

On the other hand the average case of typhoid fever in a fully protected man is very much less serious, indeed it was difficult, if not impossible, in 1915 to judge clinically in certain cases whether the infection was typhoid modified by inoculation, or paratyphoid fever. In like manner during the later years of the war the clinical picture of the average paratyphoid case was itself modified by the use of triple vaccine, so that in certain cases there was practically no clinical indication that an enteric infection was present.

For the Western Front the figures show that typhoid fever, even in protected men, was decidedly more severe than paratyphoid, the case mortality being :—

1914—	Protected typhoid	5·8 per cent.
	Paratyphoid	2·0 ,, ,,
1915—	Protected typhoid	7·5 ,, ,,
	Paratyphoid	1·6 ,, ,,

Again in 1915, according to Willcox, the Gallipoli cases showed a paratyphoid mortality of not more than 5 per cent. There can be no doubt that the rate in protected typhoid cases was higher than this.

In a disease like enteric fever, which naturally varies in severity and duration within very wide limits, it is most difficult to state in precise terms the exact effect of a measure like prophylactic inoculation ; the general lessening of severity has been established and, as would be expected, analysis of individual cases tends to show that the average duration of fever is distinctly lessened in protected persons. In the cases observed by Torrens the average duration of fever in typhoid cases was five days less and in paratyphoid cases three days less in protected than in unprotected men.

There is no necessity to describe here the clinical manifestations of typhoid fever, but the following notes describe the paratyphoid infections and their differences from typhoid fever. It may be stated, however, at once that to distinguish clinically between paratyphoid A and paratyphoid B is impossible.

It is difficult in war time to establish the actual date of infection in any given case. General experience in the recent war has shown that, whereas the incubation period of typhoid fever is usually from 12 to 16 days, it may be much shorter or much longer in the paratyphoid infections. The shortest time observed by Torrens was, apparently, five days and the longest twenty-eight. Most observers are agreed that the average incubation period for paratyphoid fever is less than for typhoid. Vincent gives it as from nine to fifteen days. Sacquépée states it may be reduced to five or six days, Lenglet from three to eight, while Miller considers from twelve to twenty days to be most usual. The length of incubation does not appear to be affected by prophylactic inoculation.

The onset of paratyphoid fever may be either gradual or sudden ; the gradual type, 20 per cent. of the cases, is rarely so gradual as in typhoid the fever usually being at its height by the fourth day. The common early symptoms are general malaise, increasing headache, pains in back and legs and chilliness. The sudden type of onset, 60 per cent. of the cases, is commonly ushered in with fainting, vomiting, or a rigor. There is yet a third type of onset affecting 20 per cent., in which a period of trifling malaise, not sufficient to interfere with the performance of duty, and probably practically afebrile, terminates on the third or fourth day by sudden collapse with high fever and obvious illness.

As a general rule the cases with a sudden onset run a shorter course than those which develop gradually.

Fortescue-Brickdale has summarized the symptoms and early signs in 385 cases of paratyphoid B as follow :—

Headache	90 per cent.	Generalized Pains ..	25 per cent.
Diarrhœa	45 ,,	Vomiting	17 ,,
Shivering	37 ,,	Cough	13 ,,
Abdominal Pain ..	32 ,,	Epistaxis	10 ,,
Backache	26 ,,	Vertigo	9 ,,
Sore Throat	4 ,,		

Labial herpes is stated to be common.

The diarrhœa is not often persistent or severe ; it occurs early in the disease and is usually replaced by constipation after two or three days. Hence in war time the patient but rarely comes under observation while the diarrhœa is present ; when he does do so the stools have a putrid odour and the appearance and consistency of the ordinary typhoid fever stool.

The shivering does not often amount to a true rigor, though repeated rigors may occur just as in typhoid. Recurrent rigors appear to be more frequent in paratyphoid A than in either typhoid or paratyphoid B. Care must, of course, be taken to exclude a coincident malarial infection. Abdominal symptoms, apart from diarrhœa, are very much less conspicuous than in typhoid ; in upwards of 70 per cent. of cases there is no abdominal pain after the first two or three days ; quite often there is none throughout the whole disease.

Sweating is frequent and sometimes causes considerable exhaustion. Epistaxis, though only noted in 10 per cent. of the cases, is probably more frequent, but is often very slight and occurs so early in the disease as to be forgotten by the time the history is taken.

The average degree of toxicity is much less than in typhoid fever, therefore the typhoid state is the exception rather than the rule. Pronounced nervous symptoms may occur, but are relatively infrequent, confusional psychoses have been described, as also hemiplegia with sensory disturbance.

Meningismus of such degree as to simulate meningitis is far less common than in typhoid fever. Often the general appearance of the patient shows nothing more striking than a slight flush, some dilatation of the pupils and a general air of heaviness, even though the temperature may be 104° F. The tongue tends to be dry and coated, with dorsal slabs of fur, and red tip and edges ; this appearance depends largely on the diet and on the hygiene of the mouth. In very severe cases the tongue is dry, glazed and cracked, just as in typhoid.

The abdomen is often normal ; sometimes there is a certain sensation as of elasticity or tumidity on palpation. Cæcal gurgling and tenderness are rare, but tenderness under the left ribs is fairly common.

The spleen is enlarged in more than 60 per cent. of cases ; it is palpable in nearly half of all the cases at some time during the illness. Quite often the spleen may not be felt until the third week or even later ; as a rule, however, the enlargement is apparent about the sixth day. Opinions differ as to whether the average splenic increase is so great as in typhoid. In the experience of Torrens the spleen of paratyphoid is harder than the spleen of typhoid, and for this reason it is easier to feel. The enlarged spleen is nearly always more or less tender, and sometimes there is perisplenitis with an audible friction rub. Fortescue-Brickdale noted a palpable spleen in 43 per cent. of his cases and the average weight in fatal cases was 6½ ozs.

Chevrel states that the liver is almost always increased in size. Miller says the liver edge is occasionally lower than normal, and pain on deep pressure over the gall bladder is fairly common. In Torrens' experience definite enlargement of the liver is rare, as also real tenderness over the gall bladder.

The urine contains albumin in half the cases, apart from any co-existent bacilluria ; this, however, does not persist long and is of no special significance.

The respiratory tract is not conspicuously affected by paratyphoid fever ; cough is present at the outset if there be initial sore throat or laryngitis ; bronchitis and nasal congestion, usually mild, are fairly common during the first ten days, especially in soldiers who have been subjected to any considerable journey after going sick. A considerable proportion of very severe and fatal cases, as would be expected, show pneumonia of lobar or more commonly of lobular distribution ; the sputum in these sometimes contains paratyphoid bacilli.

Endocarditis and pericarditis, though recorded, must be very rare ; dilatation of the heart can but rarely be demonstrated by percussion and then only in the latest stages of severe cases. Shortening of the first sound, with some loss of intensity, is not infrequent during the second and subsequent weeks. The pulse is slow for the height of the temperature, relatively more so than in typhoid, and noticeably soft often to the point of dicrotism. The blood pressure is low, 80–95 mm., and remains subnormal well into convalescence.

The temperature presents no very characteristic features. The rise may be abrupt or gradual; the maximum is rarely more than 104° F. There is not the same tendency to plateau formation as in typhoid fever, and there is commonly a daily variation of nearly two degrees which produces a remittent or intermittent type of pyrexia. The duration of fever is very variable, from a few days to many weeks; the average is difficult to state, probably about 20 days for both paratyphoid A and B. The termination is usually by lysis, but quite frequently by a form of modified crisis extending over about forty-eight hours. There is often a very marked disinclination for the temperature finally to settle down, even when convalescence appears to be well established. Recrudescences are common and true relapses occur in about 10 per cent. of all cases.

The sub-normal temperature during convalescence, which is so common in typhoid fever, is not so marked in paratyphoid infections, though it is present in a considerable proportion of cases.

The following charts illustrate paratyphoid fever. Charts I.–VI. are from paratyphoid A. Charts VII.–XII. are from paratyphoid B. All these cases were proved bacteriologically, most of them by blood culture; in none had triple vaccine been administered.

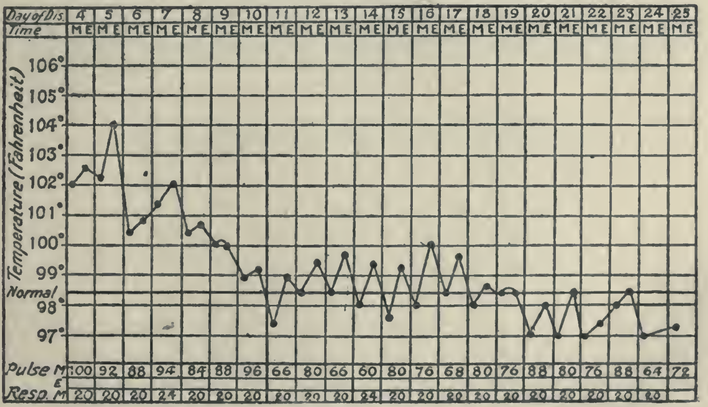

Chart I.

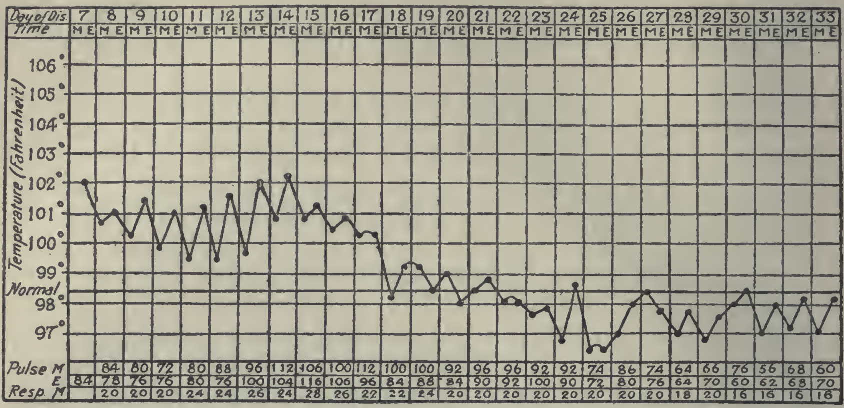

Chart II.

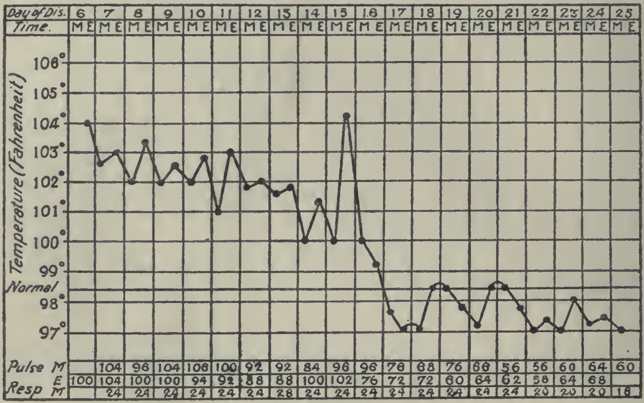

Chart III.

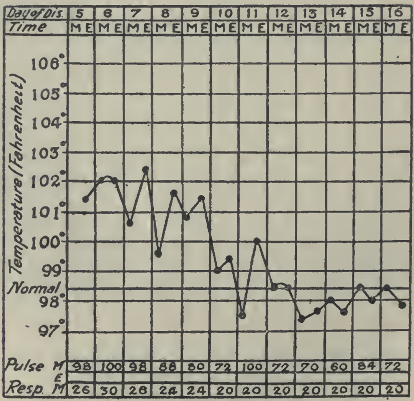

Chart IV.

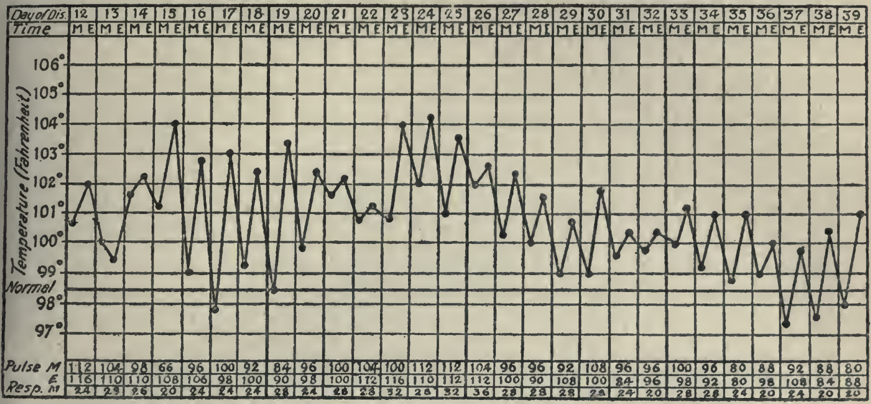

Chart V.

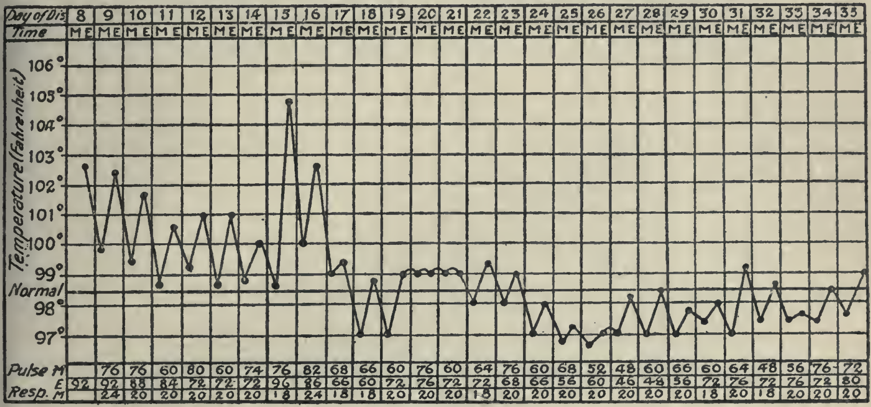

Chart VI.

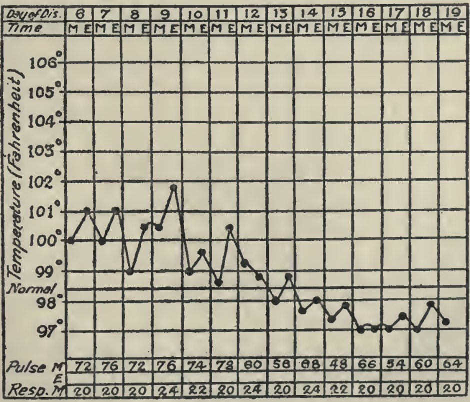

Chart VII.

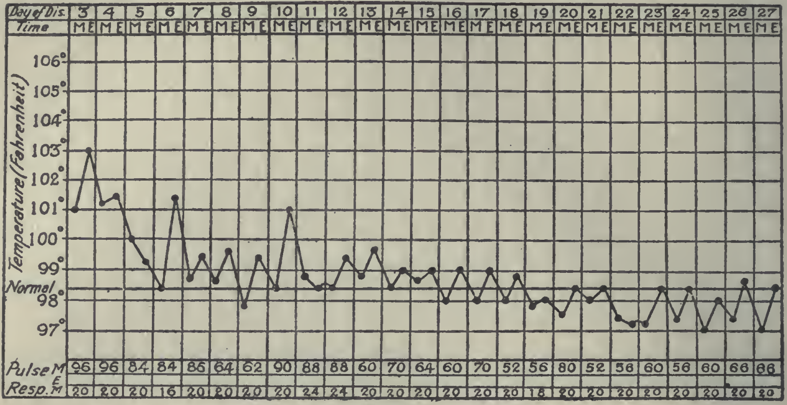

Chart VIII.

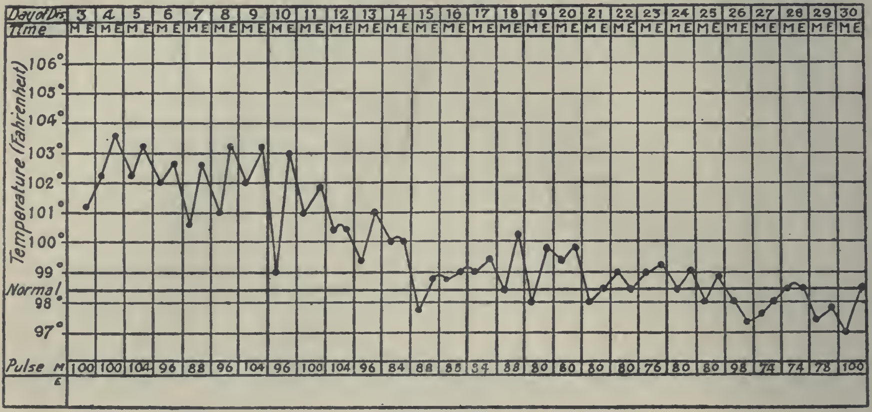

Chart IX.

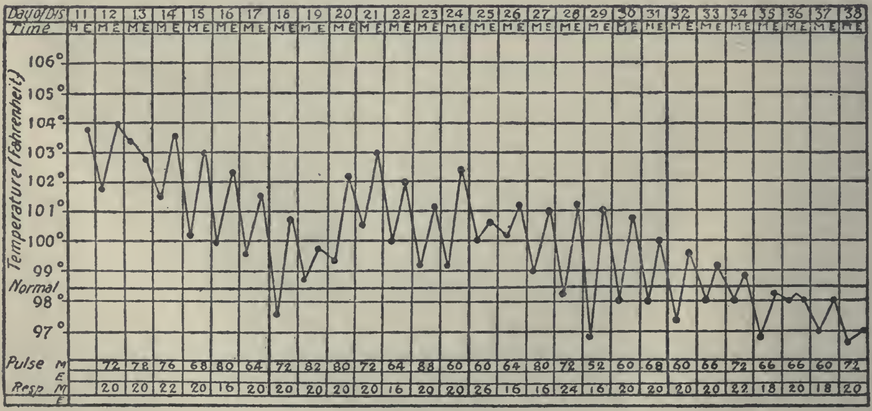

Chart X.

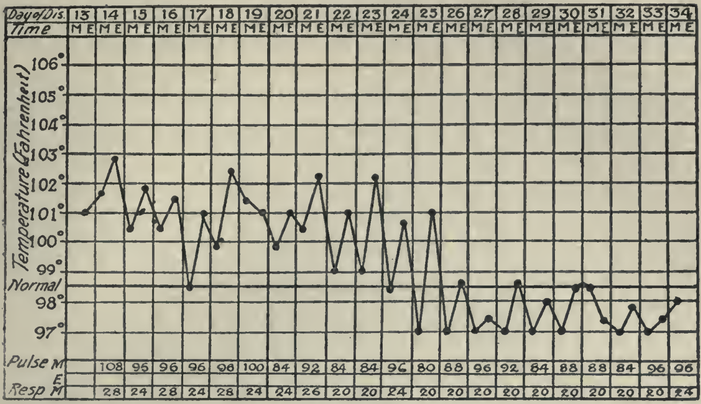

Chart XI.

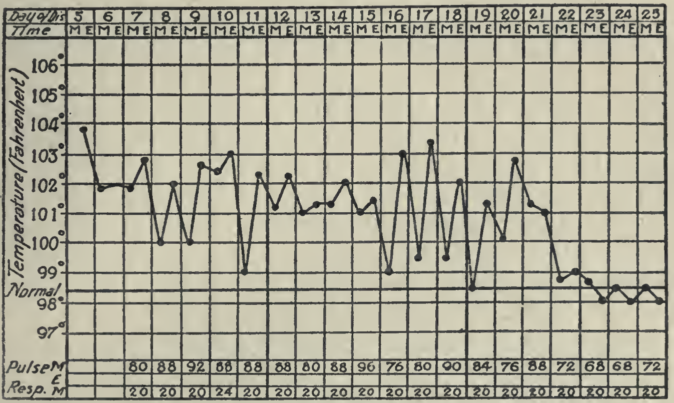

Chart XII.

The rash in paratyphoid fever is present in about 60 per cent. of cases; it does not conform so strictly to type as does the typhoid roseola. Miller describes the following varieties:—

(1) Rose-pink papules as in typhoid, occurring in successive crops, and most evident on the lower part of the chest and abdomen.

(2) Larger spots of irregular outline, red with a bluish tinge, raised, and not completely fading on pressure. This variety is characteristic of paratyphoid fever, when present; the spots may be very profuse and have been mistaken occasionally for measles, German measles, varicella, and even smallpox.

(3) A rare variety of rash, which may occur alone or in association with the other types, consisting of cyanotic sub-cuticular patches of irregular shapes and sizes and indicating a severe infection.

The spots vary in number from two or three to several hundreds; they may be noticed any time from the end of the first week well into convalescence. Their first appearance may be delayed till the temperature has been normal for several days. An analysis of several hundred cases showed that the twelfth day is the most usual date for spots to appear. A feature of most paratyphoid cases, shared with a fair number of typhoid cases that have been inoculated, is to feel and look quite well about the twelfth day of illness even though the fever continues for another fortnight.

Convalescence in paratyphoid fever, even in quite uncomplicated cases, is apt to be disappointing; all goes well till the patient gets up and about; thereafter progress is tedious. There is a great tendency for complaints to be made of persistent lassitude, headache, lack of appetite and insomnia. There is often considerable variation between morning and evening temperature and the latter may be slightly above normal. This is not an indication for further rest in bed; these cases do better if encouraged to be out of bed and taking a reasonable amount of exercise. A small but definite proportion of patients manifest true cardiac dilatation during convalescence; still more show the characteristic features of disordered action of the heart, præcordial pain, dyspnœa on exertion, tachycardia and palpitation, without any demonstrable lesion in valves or myocardium. In this last type of case there is usually vasomotor instability, as shown by cold and livid hands and feet and tendency to perspiration without cause.

Definite neurasthenia is a not uncommon sequel to paratyphoid fever, but it is hard to say how much of this depends on previous war experiences and how much, if any, is directly attributable to the specific infection.

On the whole, convalescence from paratyphoid fever differs rather strikingly from that of typhoid fever, but principally in the subjective feelings of the patient, who does not manifest that sense of well-being and eagerness to be up and doing that is so often a feature of typhoid convalescence.

From the above brief clinical description it may be gathered that paratyphoid fever, whether A or B, is a miniature edition of typhoid fever so far as the average case is concerned; it cannot, however, be too strongly emphasized that a severe case of paratyphoid fever is just as severe as the most serious case of typhoid, and that every complication or accident which may attend the latter may equally well be encountered in the former.

Serious complications are not so frequent in paratyphoid as in typhoid; minor complications are not so serious when they do occur. In a disease showing so many diverse clinical signs as paratyphoid, it is difficult to say where legitimate manifestations cease and complications begin. The preponderance in certain groups of cases of certain manifestations or complications has led some writers to attempt to classify paratyphoid fever into various clinical types; thus Miller recognizes typhoid, dysenteric, biliary, rheumatic, respiratory, influenzal, and septicæmic types.

The typhoid type is by far the most common variety, and the foregoing remarks principally apply to it.

The dysenteric type, which is only admissible when coexistent dysentery has been rigidly excluded, is relatively infrequent, but is more common in paratyphoid B than in paratyphoid A. It is remarkable that it is not more often met with in severe cases, in view of the relative frequency of considerable large gut ulceration in paratyphoid B. Paratyphoid fever can, however, begin with symptoms that clinically closely resemble those of true dysentery, so that a certain amount of hæmorrhage in quite the early days does not necessarily negative the diagnosis. At the same time, the great majority of this type of case was reported from the Eastern theatres of war, so that the possibility of double infections, especially paratyphoid grafted on to a bacillary dysentery, is difficult to exclude.

With regard to the biliary type there is great divergence of opinion as to the frequency with which infection of the bile passages and gall bladder, to the extent of causing signs or symptoms referable to these organs, may occur. Rathery comments on the rarity of jaundice or biliary symptoms in his series of 1088 cases of paratyphoid B. Torrens and Whittington state that jaundice and biliary symptoms were conspicuous by their absence on the Western Front in 1915. Torrens could not trace any special connection between the camp jaundice, which was common in Mesopotamia, and enteric fever. On the other hand, Dawson and Hume record twenty-four cases of infective jaundice attributable to enteric fever, namely, in typhoid, six cases; in paratyphoid A, four cases; and in paratyphoid B, fourteen cases.

It is probable that the paratyphoid fevers of the Gallipoli campaign were accompanied by jaundice and biliary symptoms in larger proportion than the same fevers in other areas. Morley and Battinson Smith record a case of "epidemic jaundice" which showed acute gangrenous cholecystitis; *Bacillus paratyphosus B* was recovered from the stools and bile of this patient. Sarrailhé and Clunet recovered an inagglutinable paratyphoid bacillus from the blood of a number of cases of camp jaundice in Gallipoli; subsequent investigation showed these organisms to be, for the most part, paratyphoid A.

Acute cholecystitis is met with from time to time, usually after the third week.

In the rheumatic type, acute articular rheumatism has been noted in a few cases of paratyphoid fever. Arthralgia and myalgia, without objective evidence, occur in close on 10 per cent. of cases. Nobécourt and Peyre consider articular rheumatism to be a common manifestation, especially of paratyphoid B. Synovitis simulating infective arthritis and giving rise to suspicion of gonorrhœa was noted by Miller in several cases.

In the respiratory type, rapidity of respiration may be due simply to toxæmia, but some bronchitis is commonly present. Lobar and broncho-pneumonia are seen in cases either at the onset or at any time during the course; in only a small proportion of these cases can the paratyphoid organism be recovered from the sputum, or from the lungs after death. Pleurisy is far from uncommon in paratyphoid fever; often a little dry pleurisy is noted for a few days, and clears up completely. Sometimes an effusion develops very rapidly; this may be lymphocytic in nature, and suggests a tuberculous process. On the other hand, a polynuclear effusion which rapidly goes on to empyema is not unlikely, especially in paratyphoid B. It is rare to recover paratyphoid bacilli from the simple pleural effusions, but they have been found in some of the empyema cases according to Weeks and others.

It has been suggested that paratyphoid infections may light up a latent tuberculosis; certainly lymphocytic effusions with transient signs at the apices suggesting tuberculosis have been described, but more evidence is wanted on this point. Joltrain and Petitjean noted 19 cases of pleurisy in 310 cases of paratyphoid fever; 18 were due to *Bacillus paratyphosus B* and 1 to *Bacillus paratyphosus A*, 15 were sero-fibrinous, 2 were purulent and 2 were dry.

In the influenzal type, paratyphoid fever can simulate closely the respiratory, the gastro-intestinal, or the nervous forms of influenza. This is especially the case in protected men. Isolated examples of these varieties are very likely to escape detection in a busy general hospital, since it is impossible to keep all such mild cases under observation sufficiently long to exclude enteric infections by serological tests.

The septicæmic type is rare. In it death occurs early in the disease; often there are no local lesions found *post mortem*, nothing but the general features of septicæmia. Job and Ballet record three such cases and Sawasaki has met with similar ones in Japan. Gangrene of the extremities may precede death.

Some of the complications of paratyphoid fever have been sufficiently discussed in the foregoing clinical description. There remains a large number of which only three require special notice here. Hæmorrhage occurs in less than 5 per cent. of all cases; there seems little doubt there is a greater tendency to hæmorrhage in paratyphoid B than in paratyphoid A. Perforation is definitely less common than in typhoid fever, but appears to be somewhat more frequent in paratyphoid B than in paratyphoid A. Nearly all published figures show that more than one quarter of the deaths are due to hæmorrhage or perforation. Webb Johnson gives the incidence and mutual relationship of perforation and hæmorrhage of a series of cases in France.

TABLE XIV.

	Number of cases.	Hæmorrhage.	Perforation.	Hæmorrhage and Perforation.
Typhoid	1,118	50	9	3
Paratyphoid A ..	344	1	2	0
Paratyphoid B ..	1,038	16	3	1

Apart from dilatation of the heart and the symptoms of simple disordered action, a small proportion of cases give evidence of more definite damage to the heart muscle. For example, heart block, auricular flutter and auricular fibrillation may all occur. The lesions giving rise to these phenomena may be transient or permanent, and it is important from the patient's point of view that the clinician should be alive to these possibilities in order that appropriate treatment may be instituted as early as possible. The fact that typhoid patients may die quite suddenly when apparently doing well, almost at any period of the disease, has long been recognized; the same mode of death is observed, but less frequently, in paratyphoid fever. It seems possible that the actual cause of death in these cases may be the sudden development of ventricular fibrillation.

The incidence of the remaining complications of paratyphoid, compared with the same in typhoid, is shown in Table XV., taken from Webb Johnson's report. The figures are based on the analysis of 2,500 cases of enteric fever treated in hospital at Wimereux, and it must be borne in mind that, just as the case mortality was far higher in other theatres of war, higher also, without doubt, was the incidence of the individual complications. The table, however, is of interest since it deals with a large number of cases all treated under practically uniform conditions,

TABLE XV.

Summary of Complications of Enteric Fever on the Western Front.

Disease.	Typhoid inoculated.	Typhoid not inoculated.	Paratyphoid A inoculated.	Paratyphoid A not inoculated.	Paratyphoid B inoculated.	Paratyphoid B not inoculated.	Totals.
Hæmorrhage	10=1·21%	40=13·46%	—	1=0·45%	1=0·41%	15=1·87%	67=2·68%
Perforation ..	3=0·36%	6=2·02%	—	2=0· 9%	—	3=0·36%	14=0·56%
Appendicitis ..	4=0·48%	2=0·67%	—	—	—	5=0·62%	11=0· 4%
Peritonitis ..	—	—	—	—	—	1=0·12%	1=0·04%
Splenic abscess ..	1=0·12%	—	—	—	—	2=0·25%	3=0·12%
Liver abscess ..	—	—	—	—	—	2=0·25%	2=0·08%
Suppurating mesenteric glands	1=0·12%	1=0·33%	—	—	—	1=0·12%	3=0·12%
Cholecystitis ..	4=0·48%	2=0·67%	—	2=0·90%	1=0·41%	6=0·75%	15=0·60%
Gall-stones ..	1=0·12%	—	—	—	—	1=0·12%	2=0·08%
Stomatitis.. ..	—	—	—	—	—	1=0·12%	1=0·04%
Noma	—	1=0·33%	—	—	—	—	1=0·04%
Tonsillitis	10=1·21%	4=1·34%	1=0·81%	7=3·16%	3=1·25%	12=1·50%	37=1·48%
Quinsy	1=0·12%	—	—	—	—	2=0·25%	3=0·12%
Deafness	1=0·12%	1=0·33%	—	2=0·90%	3=1·25%	1=0·12%	8=0·32%
Otitis media ..	3=0·36%	3=1·01%	—	3=1·35%	—	4=0·50%	13=0·52%
Parotitis	—	6=2·02%	—	1=0·45%	—	2=0·25%	9=0·36%
Laryngitis.. ..	2=0·24%	8=2·69%	—	—	1=0·41%	6=0.75%	17=0·68%
Lung abscess ..	—	—	—	—	—	2=0·25%	2=0·08%
Venous thrombosis	7=0·85%	10=3·36%	—	2=0·90%	3=1·25%	20=2·50%	42=1·68%
Urinary	1=0·12%	4=1·34%	—	1=0·45%	—	12=1·50%	18=0·72%
Epididymo-orchitis	—	—	—	—	—	4=0·50%	4=0·16%
Bone lesions ..	1=0·12%	3=0·01%	—	—	—	1=0·12%	5=0·20%
Arthritis	2=0·24%	—	—	1=0·45%	1=0·41%	3=0·37%	7=0·28%
Muscle lesions ..	—	3=0·01%	—	—	—	3=0·37%	6=0·24%
Other abscesses ..	7=0·85%	5=1·68%	—	2=0·90%	—	8=1·00%	22=0· 8%
Boils	3=0·36%	2=0·67%	—	—	1=0·41%	3=0·37%	9=0·36%
Erysipelas.. ..	—	5=1·68%	—	—	—	—	5=0·20%
Totals	62=7·55%	106=35·69%	1=0·81%	24=10·85%	14=5·85%	120=15·39%	327=13·20%
Cases	821	297	123	221	239	799	2500
Deaths	27	57	—	1	1	17	103
Mortality	3·28%	19·19%	—	0·45%	0·41%	2·12%	4·12%

and it shows the effect of prophylactic inoculation alike on typhoid and paratyphoid fever, as regards not only general severity but also incidence of complications.

When a number of men are exposed at the same time to the risk of infection by three specific micro-organisms, no one of which has the power of conferring immunity against the others, it is certain that mixed infection with two or all of the infecting agents will occur in a proportion which can be expressed mathematically.

A number of such cases have been recognized, but it is inevitable that many should escape diagnosis, since further work would not be undertaken as a routine in any case so soon as the presence of one infection had been established. It is probable that certain of the cases of anomalous course or of unduly prolonged duration, as well as those showing unexpected agglutination curves in fully protected men can best be explained on the hypothesis of mixed infections. An interesting case of mixed infection has been reported by Dawson and Whittington as follows :—

> The patient had a double infection by the *Bacillus paratyphosus A* and the *Bacillus typhosus*. He had thrombosis of the left femoral and left external iliac veins. Four relapses occurred. In the last relapse he had pulmonary infarction, and death was due to the subsequent severe lung affection on the 127th day from the onset.
>
> The following points are noteworthy: The patient had had no protective inoculations. Admitted on the twelfth day of the illness, he appeared to be typical of a rather severe enteric group infection, and his blood gave a pure culture of *Bacillus paratyphosus A*. The serum on this day and on the eighteenth day strongly agglutinated the stock paratyphoid A bacillus, and gave no reaction with *Bacillus typhosus* or *Bacillus paratyphosus B*. By the twenty-second day the patient was obviously improving and during this time he had a swinging temperature (rather characteristic of paratyphoid A infection) from 99° to 102°. On the twenty-third day, however, the temperature range became steadier, remaining between 102° and 104° for five days. On the twenty-fourth day the serum agglutinated *Bacillus typhosus* as well as *Bacillus paratyphosus A*. It gave the same reaction on the twenty-ninth day, but the reaction with *Bacillus paratyphosus A* had much diminished. On the twenty-seventh day thrombosis of the left femoral vein was first noted. The duration of this primary attack of fever lasted forty-eight days.
>
> The patient had four relapses with four, twenty, sixteen and ten days' pyrexia respectively. During the second relapse he was given two injections of paratyphoid A vaccine without obvious effect. In the middle of the third relapse a blood culture was negative. At the *post-mortem* a pure culture of *Bacillus typhosus* was grown from every viscus examined (gall-bladder, spleen, mesenteric gland and thrombosed vein), thus proving the presence of a second infection.
>
> The date of the second bacillary invasion is not quite clear. The agglutination reactions suggest that it was before the twenty-fourth day, but not much before the eighteenth day; also the temperature range altered on the twenty-third day. Thus it seems likely that when the patient came to hospital he had reached the twelfth day of a paratyphoid A attack and was in the midst of the incubation period of typhoid, that for a while the two infections reigned together, and later the paratyphoid A disappeared, leaving the typhoid to reign alone. The relapses were thus probably due to *Bacillus typhosus*.

The increased severity of enteric fever in the East and Near East is in part explained by the greater frequency of its association with malaria or dysentery, as well as the liability to hyperpyrexia or even true heat-stroke. Latent malaria may be lighted up, often in a virulent form, by an enteric infection, while the extra strain of even a mild paratyphoid infection may determine a fatal issue in a case of dysentery of only moderate severity. A certain number of paratyphoid A cases developed heat-stroke in Mesopotamia in the hot weather of 1916; the majority of these proved fatal, sometimes during the first week of illness. At this time ice was not available.

A number of cases of combined infection with typhoid and diphtheria was noted by the French authorities. The mortality in these was very high. The severity of this double infection was confirmed by experience of a small number of similar cases in the British forces.

Prognosis.

The prognosis in enteric fever has been shown to vary with the specific infection, with the amount of time that elapses between "going sick" and reception into a hospital for permanent treatment, with the climate, with the rigours of active service to which the individual has recently been exposed, and also with the presence or absence of protective inoculation against the particular infection which has been acquired. These factors have already been discussed; but there are certain clinical features which may lead the clinician to regard any given case as likely to do well or badly and also indicate the average duration of "invalidism." It is important to estimate the proportion of cases likely to be unfit for further military service and the probable incidence of symptoms sufficiently serious to justify a more or less prolonged pension.

With regard to the clinical features bearing on prognosis, in all enteric infections the most reliable guide as to the patient's actual state of well-being is the pulse. The quality of the pulse is significant; a pulse so soft as to be "dicrotic" betokens a relatively intense infection, but apart from the quality the all-important factor is the actual pulse rate. So long as the pulse rate is no more than 100 per minute the patient's condition is not likely to be very urgent; a pulse rate of 110 is serious and when the rate reaches 120 the prognosis becomes extremely grave. In adult male patients a pulse rate of more than 120 per minute continued for longer than 36 to 48 hours means death in all but a few very exceptional cases. The intensity of toxæmia, as shown clinically by the dry skin, flushed face and mental lethargy, has an obvious bearing on prognosis, but the importance varies with the nature of the infection and period of disease to which the toxæmia persists. In paratyphoid fever manifest toxæmia persisting after the twelfth day indicates a severe infection; for typhoid fever the same degree of toxæmia might be expected till the twentieth day.

Spots are most frequently seen in the more severe infections; but Torrens considers that, granted a severe infection, a plentiful crop of spots is of favourable import and that such a case is likely to do better than a similar case in which spots are scanty or absent.

The degree of splenic enlargement does not seem to be of special import, except in so far as a big spleen usually indicates an infection of at least moderate severity.

A high temperature, apart from hyperpyrexia which is always serious and particularly likely to occur in the tropics, is not a sign of danger unless it is associated with a rapid pulse, when the prognosis should be based on the pulse rate rather than on the degree of pyrexia.

The chief risk of a relapse is that it prolongs the period in which perforation and hæmorrhage may occur.

The complications of enteric fever, with the exception of pneumonia, hæmorrhage and perforation, influence prognosis principally as regards the probable length of invalidism required before any work can be undertaken. Pneumonia, hæmorrhage and perforation, however, are complications rather apart from all the rest; they may all three, but especially hæmorrhage and perforation, occur without any warning in the course of a case which has to all seeming been quite a mild infection. The advent of any one is of very grave prognostic import, but perforation is infinitely the most serious, since it is probable that not more than one in fifteen can be saved under active service conditions.

In a series of seventeen perforations observed, only one survived, although practically all were operated upon within a very few hours of the complication occurring. In another series perforation was responsible for 14 out of 103 deaths in 2,500 cases according to Webb Johnson.

Hæmorrhage is probably responsible for one-fifth of all deaths from enteric fever.

Invalidism.

The following table indicates the average duration of invalidism. It is based upon 2,000 cases treated in Addington Park Hospital and shows the number of days' treatment necessary for cases of enteric fever from the different theatres of war. It is noteworthy that the length of treatment appears to vary directly with the distance from England of the country where the infection was contracted.

TABLE XVI.

Duration of Treatment of Enteric Fever.

Force from which derived.	No. of cases.	Average number of days under Treatment.
France	1122	102·92
Gallipoli	143	140·59
Egypt	206	151·36
Salonika	192	152·69
Malta	117	156·44
East Africa	10	208·30
Mesopotamia	11	234·00
India	3	227·00
Miscellaneous Cases	196	126·52
Total number of Cases.	Total number of days under treatment.	Average number of days under Treatment.
2000	244,520	122·26

The average length of treatment is seen to be 122·26 days so that it is reasonable to suppose that an ordinary case is fit to resume duty six months after the date of infection. A further two to three months may have to be added to this period for those patients who were infected in the East. A small percentage of all cases become carriers and therefore useless for further military service. In the unprotected this proportion is fully 2 per cent. In those protected by triple vaccine it is probable that the proportion is much lower. The percentage of typhoid carriers is higher than that of paratyphoid, while that of paratyphoid B is higher than that of paratyphoid A.

The other principal reasons for discharge from military service after enteric fever are complications or sequelæ affecting the cardio-vascular system, and neurasthenia.

Phlebitis and thrombosis occur in not more than 4 per cent. of all cases; a small but definite proportion of these cases are left with permanent œdema of the limb and are unfit for further military service.

Disordered action of the heart is a more frequent reason for discharge, since symptoms may persist to the extent of precluding any but a sedentary occupation for several years, in spite of careful treatment by graduated exercises. Such cases, however, should not be discharged for at least a year, since a large proportion will recover under suitable conditions.

Those few cases which manifest a more definite cardiac lesion, such as heart block, auricular flutter, or auricular fibrillation are probably unsuited for further military service.

The number of soldiers now receiving pensions for disabilities which are directly attributable to enteric fever is not great, either absolutely or relatively. The only cases of this sort seen by Torrens during 1919 may be grouped under the headings general debility, disordered action of the heart, other cardiac conditions, effects of thrombosis and affections of the gall bladder. In all these, with the exception of the first, a pensionable disability may persist for many years.

Statistics are not at present available to show the exact percentage of enteric cases who were discharged from the army or who are now drawing pensions.

Diagnosis.

The diagnosis of enteric fever depends upon its clinical manifestations and laboratory investigations. With regard to the former it is established that clinical signs can take one no further than a diagnosis of enteric fever ; the attempt to say that a given case is either typhoid or paratyphoid fever can only be a guess, since typhoid can be as mild as paratyphoid, and paratyphoid can be as severe as the worst case of typhoid. This statement applies alike to protected and unprotected persons, the only difference being that the experienced observer is more likely to guess correctly in the latter case than in the former.

Any case presenting several of the characteristic enteric features—headache, continued fever, slow pulse, diarrhœa, tumid belly, spots, enlarged spleen and mental lethargy—must at once be referred to the laboratory for more precise diagnosis ; but these are not the important cases, as they would justify a clinical diagnosis anywhere, and there is no risk of their failing to be isolated for an adequate period. The important cases are those which are so mild and atypical that, clinically, they do not suggest an enteric infection, for these may well disseminate infective material should they be returned to duty while in a " carrier " condition. In the majority of cases there will be one or two isolated signs or symptoms that may put the wary observer on the track: such as, the quality of the pulse, a suggestion of undue lethargy, a history of looseness of the bowels or epistaxis at the onset of the illness, an increase in the area of splenic dullness, or a doubtful spot or two about the shoulders or abdomen.

It is well to remember that in the tropics malaria is more often confounded with typhoid than with any other disease.

In view of the large number of cases which are not enteric, and in which the diagnosis of pyrexia of uncertain origin can never be replaced by one more scientific, as well as a host of trench fever and influenza cases, it is obvious that the ideal method of treating every case of unexplained fever of six days' duration as suspected enteric group is not practicable. Actually then the onus of diagnosis rests on the clinician, who must appreciate that any case of unexplained fever may be enteric, and who must be unceasingly alert to distinguish those lesser signs which may lead him to seek the aid of his bacteriological colleague only in those cases which will yield a reasonable proportion of positive results.

The atypical forms only of influenza or trench fever are likely to give rise to doubt and may be clinically indistinguishable from the modified varieties of enteric fever. An enumeration of leucocytes may serve to eliminate a certain number of "suspect" cases; a definite leucocytosis excludes enteric fever, while a true leucopenia, (4,500 cells or less), is very suggestive of an enteric infection, especially when associated with a definite mono-nuclear increase. A mono-nuclear leucocytosis may persist throughout convalescence. Counts of from 5,000 to 7,000 white cells are, however, often found in influenza or trench fever.

The atropine test, introduced by Marris, is a useful aid to diagnosis, but its value lies chiefly in the fact that a series of negative results excludes enteric fever; unfortunately it has been found that a positive result may be obtained in about 20 per cent. of cases of trench fever and possibly other febrile disorders as well, certainly also in cases of infection by *B. aertrycke*. The test depends on the variation in the pulse rate of the suspect after the hypodermic injection of 1/33 gr. of atropine sulphate. The injection is given one hour after a meal, the patient being recumbent, the pulse is counted every minute till it is of uniform rate, the atropine is injected and the pulse rate noted minute by minute for from 30 to 35 minutes. The maximum increase due to the atropine is thus ascertained. If the increase does not exceed 14 beats per minute, the reaction is positive. The test is applicable from the fifth to fourteenth day of fever; it is not reliable when the initial pulse rate is over 100 beats per minute and should not be employed in patients over 50 years of age or those who are markedly arterio-sclerotic.

It is thus possible by clinical means to earmark two classes of cases, first those that can be considered as certainly enteric fever, and secondly those that must be regarded as suspect cases till the diagnosis can be confirmed or refuted. Both classes must be referred to the bacteriologist without delay for confirmation and for the identification of the specific infective agent. Topley, Platts and Imrie claim that about 5 per cent. of the cases invalided from the Western Front as pyrexia of uncertain origin were in reality suffering from enteric fever ; it is probable, however, that this figure is too high.

Cases of disease due to the food poisoning group of organisms, *Bacillus enteritidis, Bacillus aertrycke* and *Bacillus suipestifer,* can generally be diagnosed clinically from enteric fever by the sudden onset with severe diarrhœa and vomiting, the occurrence in epidemic form of several cases at exactly the same time, the short duration of fever and the absence of the classical features of enteric fever. Perry and Tidy, discussing an extensive epidemic due to *Bacillus aertrycke,* noted a latent period of 6 to 28 hours, sudden onset with diarrhœa and abdominal pain in many cases apyrexial, fever when present rarely lasting more than two days, tongue clean throughout and stools watery with but little fæcal matter.

A considerable epidemic of disease due to *Bacillus suipestifer* was noted in Egypt in 1917. The cases resembled in the main those due to *Bacillus aertrycke* but vomiting was more pronounced a feature and the temperature remained high for 96 hours, thereafter falling by crisis.

With regard to laboratory diagnosis this is easy in unprotected persons. The specific bacillus can be recovered from the blood in most cases up to the fifth day and often for longer. If the blood fails, cultivation of the stools or urine will often give a positive result in the second and third weeks of the disease.

In war time it often happens that cases do not get within touch of a properly equipped laboratory till the second week or later ; it is then necessary to test for specific agglutinins in the patient's blood serum. In a positive case these will appear from about the tenth to the twelfth day, though the paratyphoid A agglutinins may be delayed till the third week.

In protected individuals the procedure is less simple because the percentage of cases in which the specific organism can be recovered from the blood, urine or fæces is much less, and the act of inoculation causes the specific agglutinins for the organisms, against which the person has been protected, to appear in the blood serum, quite apart from any infection having taken place.

It has been shown, however, that by the use of special technique and standard bacillary emulsions, as advocated by Dreyer, a positive diagnosis can be made in nearly every case by noting the variations in agglutination titre to the different organisms exhibited by the patient's blood serum throughout the course of the disease.

Infections due to *Bacillus enteritidis* may closely resemble some cases of paratyphoid B fever; this organism possesses identical biochemical reactions with *Bacillus paratyphosus B* but can be distinguished readily by agglutination tests.

Infections due to *Bacillus aertrycke* or *Bacillus suipestifer* are more difficult, as their biochemical and agglutination reactions are the same as for paratyphoid B. Absorption tests, however, serve to differentiate *Bacillus paratyphosus B* from the others.

The diagnostic position of enteric fever may be summarized as follows :—

A diagnosis of enteric fever may be justified on purely clinical grounds even though unsupported by bacteriological or serological findings. The percentage of cases thus unsupported will be small, probably less than 5 per cent. in those protected by triple vaccine, and practically negligible amongst unprotected men, provided they are under observation sufficiently long for a series of agglutinations to be determined. An additional factor which applies also to unprotected men is the occurrence of infections by bacilli closely allied to, but not really belonging to, the typho-paratyphoid groups as at present defined.

The isolation of one of the specific bacilli from the blood is the simplest and most conclusive proof of infection. This should always be attempted as soon as enteric fever is suspected. *Bacillus typhosus* has been recovered by Torrens from the blood on the 26th day of illness quite apart from a relapse. Recovery of the bacilli from the stools or urine is the next most satisfactory proof of infection; this procedure is most successful in the second, third, and fourth weeks of the disease.

If no bacilli can be recovered in those protected by triple vaccine, the accurate diagnosis must depend on the agglutination curves of the patient's blood serum, as determined by three, four, or more successive readings at intervals of three, four, or five days. A variation of 150 to 200 per cent. or more in the agglutination titre to one of the bacillary emulsions between the twelfth and thirtieth days of illness implies an infection with that bacillus. A variation of as little as 100 per cent. is probably sufficient but may just fall within the limit of technical error. In unprotected men agglutination with any of the three bacilli in higher serum-dilution than 1–10 is proof of infection with that bacillus; in the case of paratyphoid A a positive diagnosis is justified even if the maximum titre is no more than one in ten. To take these agglutination readings it is essential to use standard agglutinable bacillary emulsions, to use the macroscopic method and to follow closely the technique laid down by Dreyer and Ainley Walker.

Treatment.

With regard to the general treatment of enteric fever the experiences of the war have done nothing to modify the old-established methods. The essential factors still remain, namely, good nursing, careful dieting, and enforced rest at the earliest possible moment in the nearest hospital set apart for the treatment of these cases. It cannot be too strongly emphasized that there is nothing so prejudicial to the interests of the patient as repeated transference from place to place or even from one ward to another in the same hospital.

It is generally agreed that only fluids and jellies should be permitted during the height of the disease, with the possible addition of milk-chocolate and rusks after the tenth day in mild non-toxic cases ; there is, however, a tendency to permit solid food to cases of paratyphoid fever relatively early in the disease. Nothing is probably gained by this course, and it is safer to adopt the old rule that no case should have solid food till the temperature has been normal for seven days ; the convalescence of cases treated in this manner is speedier and less interrupted by relapses than when solids are permitted at an earlier stage. It is of the greatest importance to encourage the patient to drink as much water as possible during the height of the disease.

No drug is of specific value in the treatment of enteric fever. An aperient should be administered if the case is constipated and seen in the first ten days ; after this date the bowels should be opened, if necessary, every other day by the administration of an enema of normal saline. Antipyretics and intestinal antiseptics are best avoided. Liquid paraffin may be given with advantage throughout the disease so long as there is no diarrhœa, as it tends to minimize the constipation which is often so obstinate during convalescence. Bromide is of service if insomnia is troublesome.

Stimulants are but rarely necessary or desirable until convalescence ; the pulse must be the guide. It appears that very severe cases can be kept alive a few hours or days longer than would otherwise be the case by the free exhibition of brandy, but that rarely, if ever, is a fatal issue avoided by this means. This does not apply to cases who have developed pneumonia or who have been operated on for perforation ; or to the occasional administration of a tablespoonful of whisky in a little warm milk to induce sleep.

The foul condition of the mouth and the characteristic typhoid tongue can be greatly improved by careful attention, especially by encouraging the patient to use "chewing gum" which is an excellent prevention of the septic parotitis so frequently occurring in typhoid fever.

Immersion in baths can rarely be practicable in wartime, even if it be desirable. Tepid or cold sponging is, however, of the greatest value; it should be done as a routine measure every four to six hours to all patients whose temperatures are 103° or over. Apart from the degree of pyrexia, sponging is the most valuable remedy for restlessness or insomnia.

With regard to the treatment of complications, meteorism is best treated by stopping milk and allowing only whey or albumen water for 48 hours or longer. A simple enema may be of service; the turpentine enema should be used with caution and not during the third week of the disease, since there is no means of estimating the extent of ulceration in the large intestine.

Immediate operation offers the best chance in cases of perforation. Peritonitis without perforation may be localized and unsuspected clinically; such cases often recover. If generalized, operation should be undertaken as soon as the diagnosis is made.

In the event of hæmorrhage occurring all fluids should be stopped for at least 48 hours and sufficient morphia injected to keep the patient absolutely at rest. The mouth must be carefully attended to during this time. Feeding, when recommenced, must proceed with the utmost caution. It is amazing what a large amount of blood can be lost without death ensuing. One large hæmorrhage is often less serious than a series of smaller ones. When the hæmorrhage seems definitely to have ceased, subcutaneous infusion with saline solution up to 30 oz. may be permitted, if the condition of the patient remains unsatisfactory; and this may be repeated if no further bleeding takes place. It is well to attempt to anticipate the occurrence of hæmorrhage by increasing the coagulability of the blood about the time when the sloughs may be expected to separate. For this purpose 30 gr. of calcium lactate may be given thrice daily from the sixteenth to the twentieth day of typhoid fever and from the fourteenth to the eighteenth day of paratyphoid fever. In a considerable number of cases treated in this manner, and checked by controls not so treated, the results appeared distinctly to justify the measure; hæmorrhage was less frequent and, when it did occur, of less severity.

In cases of thrombosis the administration of citrates is indicated. Marris claims excellent results from the intravenous injection of 10 oz. of 5 per cent. sod. citrate solution.

Pulmonary complications must be dealt with on their merits.

Cholecystitis and gallstones may require surgical intervention. The former will usually yield to aspirin and urotropine.

In addition to these general methods, certain special methods of treatment have to be considered.

Various writers have advocated from time to time the therapeutic use of vaccines in enteric fever. A great variety of different forms of vaccine have been employed, varying from stock killed cultures, as used for prophylactic inoculation by Wiltshire and MacGillicuddy, to an autogenous living vaccine used by Bourke, Evans and Rowland. The dosage has varied within wide limits and the vaccine has been given subcutaneously, orally, or intravenously. In most cases the evidence adduced in favour of vaccine treatment fails to carry conviction. The cases are few in number and there is no record of specially selected similar control cases treated at the same time without vaccines.

In January 1915, Torrens believed he was favourably influencing certain cases by injection of stock antityphoid vaccine; many of these cases were later proved to be paratyphoid fever running their normal course. Subsequently, a considerable experience of vaccines both stock and autogenous led him to the belief that equally good results were obtained in both typhoid and paratyphoid fever without the use of such vaccines as he was able to procure. As regards the use of stock antityphoid vaccine for cases of *Bacillus typhosus* infection, Whittington has shown in a careful analysis of controlled cases that the results are no better with vaccine than without it, that there is " a distinct suspicion that the vaccine increases the incidence of hæmorrhage," and that neither the duration of the fever nor the occurrence of complications is appreciably altered.

It thus appears that there is not sufficient evidence to justify a dogmatic opinion on the value of vaccine treatment in enteric fever, but the probability is that it is of little value as hitherto practised, while it is certain that its beneficial effect is by no means striking.

Serum treatment, promising though it seems on theoretical grounds, does not appear to have been discussed in English medical literature, although it has been used in France.

Prevention.

The measures employed for the prevention of enteric fever were prophylactic inoculation and general measures of hygiene and sanitation. In August 1914, in conformity with the usual procedure by which troops were not inoculated against enteric fever until they were proceeding on service abroad, only a small proportion of the troops forming the expeditionary force was protected by inoculation at the time war was declared. But the work of inoculation was carried on energetically after the expeditionary force arrived in France, and eventually the proportion of inoculated men exceeded 90 per cent. The progress of events during the five years of the war has proved conclusively that it is the best, most important and successful means at our disposal for combating typhoid fever. Inoculation and systematic re-inoculation at stated intervals should be rigidly enforced in every army. The success of anti-typhoid inoculation was assured by the autumn of 1915, and the question then arose as to the advisability of introducing a similar measure to deal with the paratyphoid fevers which threatened to become a distinct menace to the health of the army.

In January 1915 inoculation with triple vaccine was adopted as a routine for all the British expeditionary forces. One c.c. of vaccine contained 1,000 million of *Bacillus typhosus* and 750 million each of *Bacillus paratyphosus A* and *B*. Two injections were given at an interval of eight to ten days, the first dose being 0·5 c.c. and the second 1·0 c.c.

It was also ordered that re-inoculation, one dose of 1 c.c., should be performed as a routine measure after an interval of from eighteen months to two years. It had been shown that the result of simple anti-typhoid inoculation was not only to reduce the incidence of typhoid fever but also to diminish the severity of the infection when acquired, as well as the liability to complications; but it was possible that some of these beneficial effects might be impaired or abolished by the addition of paratyphoid bacilli to the vaccine. In the event, however, the experiment was amply justified; the incidence of each infection steadily decreased year by year and was always conspicuously less in those who had been protected by inoculation. The death rate per 1,000 of ration strength was also consistently lower for each infection amongst the protected, as also the case mortality per cent., except for paratyphoid in 1918, when, however, there were too few cases to afford reliable evidence.

The increase in the case mortality from typhoid fever in 1917 and 1918 occurs in both protected and unprotected; it therefore probably depends on other factors rather than on the adoption of triple vaccine. This has been referred to above, and even if it could be shown to depend entirely on triple vaccine the disadvantage would be many times counterbalanced by the very much lower incidence of the enteric infections in protected persons. The efficacy of prophylactic inoculation is shown in the following table, taken from the official returns for the Western Front from 1914 to 1918.

TABLE XVII.

Comparative Statistics amongst Protected and Unprotected Men.

Theatre of War.	Year.	Disease.	Incidence per 1000.		Death rate per 1000.		Case Mortality per 1000		No. of Cases.	
			Protected.	Unprotected.	Protected.	Unprotected.	Protected.	Unprotected.	Protected.	Unprotected.
France	1914	Typhoid ..	—	—	—	—	5·8	17·3	51	202
		Para. A ..	—	—	—	—	—	—	—	5
		Para. B ..	—	—	—	—	—	3·2	—	31
	1915	Typhoid ..	·93	8·1	·07	1·8	7·5	23·2	517	288
		Para. A ..	—	·4	—	·003	—	·7	—	281
		Para. B ..	—	1·7	—	·03	—	1·9	—	1043
	1916	Typhoid ..	·57	·51	·009	·04	1·58	8·33	693	36
		Para. A ..	·21	3·19	·003	·05	1·56	1·78	256	224
		Para. B ..	·3	9·2	·002	·07	·82	.77	362	647
	1917	Typhoid ..	·104	1·09	·008	·13	7·7	12·12	194	33
		Para. A ..	·07	1·12	·000	·03	—	2·93	139	34
		Para. B ..	·18	4·14	·003	·13	1·7	3·20	346	125
	1918	Typhoid ..	·02	·19	·003	·04	13·84	24·00	65	25
		Para. A ..	·01	·04	·000	—	2·7	—	37	6
		Para. B ..	·05	·22	·000	—	·78	—	127	29

It will be seen from this table that the influence of protective inoculation on the liability to infection from enteric fever is undoubted, and equally undoubted is the very much lower case mortality in typhoid fever. It is difficult to say from these statistics whether triple vaccine has any pronounced effect on the case mortality of paratyphoid fever. The 1917 figures suggest that it had, but the 1918 figures do not confirm this. It must be noted, however, that in this latter year the total number of cases of paratyphoid fever on the Western Front was too few to be of much value. Only two deaths occurred, one in paratyphoid A and one in paratyphoid B, and it is probably quite accidental that both these happened in protected men. The incidence of complications seems to be lowered in all three infections by the use of triple vaccine.

Since one result of infection by one of the organisms of enteric fever is the appearance of specific agglutinins in the patient's blood serum and identical agglutinins are produced by the injection of the appropriate vaccine, it is reasonable to suppose that the amount of agglutinin to *Bacillus typhosus*, *Bacillus paratyphosus A* and *Bacillus paratyphosus B*, respectively present in the blood serum after prophylactic inoculation with triple vaccine, affords some approximate idea of the relative immunity conferred against each of the three infections. It must be remembered, however, that the infections themselves do not produce identical amounts of agglutinin in every case and that the response to paratyphoid A is habitually very much less than that to either paratyphoid B or typhoid; so that a quite low agglutination titre to paratyphoid A might conceivably indicate the same actual degree of immunity as a much higher agglutination titre to paratyphoid B or typhoid.

It might appear from the preceding remarks that prophylactic inoculation was the only necessary preventive measure against enteric fever. This is far from being the case, and the success of the campaign against enteric fever has been in no small measure due to the unremitting care and energy of the army sanitary authorities.

For the details connected with the diverse sanitary measures rendered necessary by the varying features of the different campaigns, reference must be made to the volumes on the Hygiene of the War; but the general principles may be summarised here.

The water supply must be beyond reproach; in the case of the trenches this can best be secured by the daily provision in tins of an adequate supply which must be chlorinated before use, or by the individual use of bisulphate of sodium tabloids. Water which has not been either boiled or sterilized in this manner must be used for no personal purpose whatsoever. Behind the line the precautions must be equally strict; but it is, of course, easier there to arrange for the provision of large tanks of properly chlorinated water. All vessels used for the carrying of water for cooking and for washing up must be kept scrupulously clean and covered up. In European countries the town water supply usually requires careful testing and supervision. At Rouen, Boulogne and elsewhere in France the supply was by no means safe, and it was found necessary to install a chlorinating plant at the source of supply.

In the Eastern theatres of war the troops may often be compelled to rely on a single water supply such as a river with its subsidiary canals; such water is highly dangerous and should only be used after sedimentation or clarification with alum and chlorination or after prolonged boiling. Since it may often be necessary for large bodies of mobile troops to be several hours out of reach of their own water supply, the utmost care must be taken to ensure that their water bottles are clean, properly corked and as large as possible. Tablets of bisulphate of sodium may be issued when there is a likelihood of temporary shortage of chlorinated water; these destroy cholera vibrios and all bacilli of the coli group in twenty minutes. It is customary to drink large quantities of soda water in the East, and the very strictest supervision is necessary over all soda-water factories to ensure that the returned bottles are properly washed in chlorinated water before being refilled, and that only properly sterilised water is used for aeration.

At the base and behind the line all excrement should be burnt in an incinerator; the urine pails should be emptied twice daily into a suitable soakage pit. In the vicinity of the front line deep trenches must be dug when practicable, and should be covered with a board to exclude flies. The site of all ground used for this purpose must be carefully marked to prevent its being used again. All urine must be passed into special tins which are emptied regularly into properly constructed soakage pits. Cresol should be placed in every tin before it is used. In permanent camps urine must be disposed of in soakage pits or evaporated in incinerators.

Latrines and cookhouses must be rendered fly-proof as far as possible by the use of canvas screens, wire gauze, etc. Special attention must be directed to the breeding places of flies, and manure must be suitably treated and disposed of.

Vegetables and fruits must not be eaten uncooked except after efficient cleansing in pure water.

Every case suspected to be enteric fever should be notified, isolated at once, and sent without delay to a hospital for infectious diseases. The occurrence of a sporadic case should lead to strict investigation as to a possible carrier in the troop or company. Spot maps must be kept of all cases and their probable place of origin. Every patient should be kept isolated until he is definitely proved not to be a carrier.

In the event of an outbreak of enteric fever in the civilian population of a town or district necessarily occupied by troops, special hospitals must be provided and all cases should be compulsorily sent to them. Infected houses and areas must be recognized and placed strictly out of bounds. Immediate notification to the sanitary authorities of all suspects is essential. The efficiency of the measures outlined above depends very largely on cordial co-operation between the combatant and the medical or sanitary authorities. This co-operation will be very much closer if steps are taken to explain the reason for the various rules and regulations. This can readily be accomplished by means of an occasional short address by the medical or company officer.

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Note.—Vincent and Muratet also quote Chevrel, Joltrain and Petitjean, Lenglet and Sacquépée, and Miller quotes Sawasaki, to all of whom reference is made in the text of this chapter.

CHAPTER III.

DYSENTERY.

THE subject of dysentery is very extensive and comprises the knowledge of a considerable number of parasites, bacterial, protozoal and metazoal, which may cause inflammation and ulceration of the intestinal canal. The term "dysentery" is in many ways inappropriate and indicates solely the passage of blood and mucus in the stools accompanied by abdominal pain and tenesmus, symptoms which are common to several infections specifically distinct. The war presented an opportunity hitherto unrivalled for the study of bowel diseases, and this has been made full use of by bacteriologists and protozoologists. Notable advances in our knowledge of these subjects have been recorded by workers attached to the British forces.

Intestinal disorders, especially dysentery, furnished a considerable proportion of casualties on all fronts ; more especially was this the case in the tropical and subtropical theatres of war. In Gallipoli, Salonika, Egypt, Palestine, Mesopotamia, East Africa, and even in France and Flanders, dysentery at different times and seasons raged in epidemics of great magnitude, and as a cause of invaliding and death it supplanted the enteric fever of British troops in more recent wars, though, taking the magnitude of the forces into account, there is no evidence to show that its incidence was higher than in the South African War.

So far as figures are available the incidence of dysentery in British Expeditionary Forces is shown in the following table :—

Table of Incidence of Dysentery (both Bacillary and Amœbic), 1914–1918.

	Aug.–Dec. 1914		1915		1916		1917		1918	
	Total Cases	Ratio per 1000	Total Cases	Ratio per 1000	Total Cases	Ratio per 1000	Total Cases	Ratio per 1000	Total Cases	Ratio per 1000
France ..	11	·05	20	·03	5,754	4·09	6,031	3·76	12,211	·79
East Africa ..							9,369	486·56	1,646	116·51
Salonika ..					5,987	63·89	5,842	28·89	9,318	58·23
Italy ..									897	9·54
Egypt ..					5,599	31·19	4,341	23·13	4,906	21·80
Mesopotamia					1,839	50·94	4,960	60·34	5,445	51·12

Three types of dysentery, correlated to three different kinds of parasites, are now recognized. They are not mutually exclusive ; one type may be superimposed upon and complicate another. The principal types and their associated parasites are as follows :—

Bacterial	Bacillary or epidemic dysentery. *Bacillus dysenteriæ* (Shiga and Flexner–Y).
Protozoal ..	(*a*) Amœbic dysentery and hepatic abscess (amœbiasis). *Entamœba histolytica.* (*b*) Balantidial dysentery. *Balantidium coli.*
Verminous ..	(*a*) Bilharzial dysentery. (*Schistosoma mansoni, S. hæmatobium* and *S. japonicum*). (*b*) " Dysentery " associated with *Œsophagostomum apiostomum, Ascaris lumbricoides,* and *Ankylostoma duodenale.*

Of these only the first two are of military importance, namely, the epidemic or bacillary, and the endemic or amœbic forms. They require, therefore, more lengthy consideration ; the remaining types, together with the other conditions which they may simulate, are of importance chiefly in connection with differential diagnosis.

BACILLARY DYSENTERY.

The characteristics of bacillary dysentery are the acuteness of its onset, a well-marked initial pyrexia, severe abdominal pain and tenesmus, the presence of *Bacillus dysenteriæ* in the stools, and a tendency of the disease to occur in epidemic form. After recovery from the initial attack, there is little tendency to relapse. The pathological process consists of an initial diphtheritic necrosis of the large intestine, together with a toxæmia of varying degree.

This type of dysentery was prevalent throughout the whole war. It first claimed serious attention when it broke out in epidemic form in Gallipoli in August 1915, where in three months it was responsible for a high proportion of the 120,000 casualties evacuated from the Peninsula on account of sickness.

From that date onwards it was much in evidence in all the Eastern theatres, being responsible for at least 90 per cent. of the acute clinical dysentery recorded.

In France and Belgium a milder form of bacillary dysentery commenced in July 1916 and reached its maximum in September of that year; similar epidemics also occurred in the autumn of the succeeding two years of war. The maximum incidence recorded was 126·62 cases per 100,000 troops in September 1916.

In the other theatres of war it was also prevalent: the admission rate to hospital per 100,000 of ration strength varied from 7,900 in Mesopotamia in 1916 to 1,300 in Egypt and 990 in Salonika in 1919; it exhibited also a distinct seasonal incidence, occurring in epidemic form as a disease of the late summer and autumn with a maximum prevalence in October, though minor outbreaks were noted during the spring months of March and April. Sporadic cases were apt to occur throughout the whole year; but, on the other hand, during the hot summer months in Macedonia, Egypt, and Mesopotamia, the disease was almost entirely in abeyance. The case mortality rate is difficult to estimate; probably it assumed its greatest virulence during the Gallipoli epidemic, though even there the death rate cannot have exceeded 5 per cent.; statistics show that in Macedonia, Egypt and Mesopotamia from 1915 onwards it rarely exceeded 2·7 per cent.

The true importance of this disease, as a military factor, is not to be reckoned solely from the point of view of the death rate, but from the amount of invalidism it causes, for in individuals recovering from a severe attack the mucous membrane of the intestine may be so damaged as to render them unfit for further service.

Ætiology.

With regard to its ætiology, circumstances which predispose to the development of bacillary dysentery are just those which are unavoidable under the conditions of modern warfare; that is, close contact of one man with another, physical exertion, a monotonous diet of preserved food, and one must add to these another factor upon which sufficient importance does not seem to have been laid, namely, the mechanical irritation of the intestinal mucous membrane by dust or sand ingested in the food. In desert warfare, or in arid regions such as Gallipoli and Egypt, it is almost impossible at times to avoid swallowing a considerable amount of sand with the food. This in itself is sufficient to produce a lienteric diarrhœa and so prepare the way for the activities of the dysentery bacillus, which is mainly disseminated by means of flies and polluted water.

The first outbreak of dysentery on a large scale in France occurred during the first battle of the Somme, when the British occupied ground from which the enemy had been driven. It was known at the time that dysentery was prevalent in his lines, and it was suspected that one source, at any rate, of the disease was the contamination of this ground. In 1918 dysentery prevailed at the time of the British advance under the same conditions. Indeed, at every phase of active movement and almost at any time in the fighting line, sanitary regulations could hardly be carried out with complete accuracy. Latrines could not be dug or kept so well as desirable, garbage and fæces could not be burnt, and the provision of water was often difficult. Under the latter difficulty the use of disinfecting water tablets was largely increased. Experience goes to show that all these dangers are increased when enemy lines are captured and occupied.

Another cause that temporarily predisposed towards increasing the spread of the disease was found in the crowded state of the infantry base depots in France. Camps designed for 1,200 men sometimes contained between 2,000 and 3,000. In the event of carriers being present—an accident which, in spite of all precautions, occurred and always will occur—such conditions of overcrowding materially aided the spread of the disease.

It is known that epidemics occurred amongst British prisoners of war in Germany, a fact which was brought to the notice of the War Cabinet by the Admiralty, War Office, Air Ministry, Colonial Office and Prisoners of War Department in a special joint memorandum dated 25th September, 1918.

The dysentery bacillus was discovered in Japan in 1897 by Shiga, and in 1900 an organism, morphologically similar, but differing in its power of fermenting mannite, was isolated by Flexner in the Philippines. Since that date a great deal of attention has been paid to this subject, with the result that many variants of these two organisms have been described. The bacteriology of bacillary dysentery attracted a considerable amount of attention during the war. Interest centred chiefly around the mannite-fermenting bacilli first described by Flexner and afterwards elaborated by Hiss and Russell, Strong and others. This work was important mainly from the point of view of laboratory diagnosis and the preparation of effective anti-sera, and it was undertaken by Murray, Gettings, Dudgeon, Andrewes and Inman.

The species of bacteria which are now recognized in bacillary dysentery are: Shiga's bacillus, the Flexner-Y group of bacilli, and certain atypical bacilli.

Shiga's bacillus, fermenting glucose only amongst the sugars and alcohols* employed as tests, and forming no indol, has been abundantly proved to be the cause of dysentery. Being much the most toxic of dysentery bacilli, it is responsible for the most serious cases and for the greater number of fatalities. It was recorded commonly from all theatres of war. In the East it accounted for about half the number of cases and showed no special epidemic prevalence; in France and Belgium, on the other hand, it apparently played a minor part, on the whole accounting for 15 per cent. of the dysenteries. It predominated at the commencement of the epidemic in August and September 1916, but was more or less replaced by Flexner bacilli later on in the late autumn. In about 2 or 3 per cent. of bacteriologically diagnosed cases both Shiga and Flexner bacilli co-existed.

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* The fermentable substances of real service in the classification of the dysentery group are four in number: glucose, mannite, lactose and dulcite.

The Flexner-Y group of bacilli apparently belongs to a single species, fermenting glucose and mannite, but not lactose or dulcite. As in the case of the former organism, the evidence connecting this species with dysentery is complete. The researches of Gettings, Murray, Andrewes and Inman undertaken on a large scale have indicated that serological races of the species exist. It may be regarded as a group formed of at least four distinct antigenic components which have been provisionally lettered V, W, X and Z. Any of these four components may so preponderate in different strains as to impart a distinct serological facies. The corresponding agglutinins are not mutually absorbed, except in a slight degree. In addition to the four serological races thus defined, there remains the true Y bacillus of Hiss and Russell, which presents differences in its agglutinability and agglutinogenic capacities. These bacilli are not nearly so toxic as is Shiga's bacillus and are responsible for the milder and more chronic forms of the disease, though occasionally they may become virulent and cause death. That is to say, two species, namely the Shiga and the Flexner-Y bacilli of various serological races, are responsible for the vast majority of cases of bacillary dysentery.

Other organisms which have been described during the war* and have been called atypical bacilli are bacilli resembling Flexner's bacillus but fermenting dulcite and separable from the latter on serological grounds, and a bacillus resembling Shiga's in its sugar reactions, but forming indol and not agglutinating with Shiga antiserum, first described by Schmitz, in Austria, as the cause of dysentery and apparently identical with the *B. ambiguus* of Andrewes and the one described by Remlinger and d'Herelle. Together with these may be grouped organisms which ferment lactose early and differ serologically from the Flexner-Y group. There is no evidence for inculpating either of these groups, and they may be classified as "atypical" or "inagglutinable" strains.

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* Dumas has lately shown that the atypical organisms may be distinguished further by their power of producing fluorescence in media impregnated with neutral red, as well as by reduction of 1 per cent. lead acetate, thereby producing a black line in a stab culture of agar containing this substance.

These latter need not claim the serious attention of the expert bacteriologist, though they constitute a source of fallacy to the beginner.

Morbid Anatomy.

With regard to the morbid anatomy of bacillary dysentery, the gross pathological appearances of the organs vary considerably according to the acuteness of the process in different individuals, and indeed in different epidemics, though the underlying process is essentially the same in all cases. It is probable that no such opportunity has ever before presented itself for studying the effects of the dysenteric toxins upon the intestinal mucosa as was afforded to pathologists in the Eastern theatres of war. In mild cases it is naturally difficult to define the exact appearances of the earliest lesions; the inflammatory changes originate in the first instance in the solitary lymphoid follicles of the large intestine. From these, superficial "snail track" ulcerations spread across the bowel, especially upon the free transverse folds, and the surrounding mucous membrane is involved in a greater or lesser degree with hypersecretion of viscid mucus. The abdominal viscera do not exhibit any striking changes.

In very acute cases, succumbing to an overwhelming infection, the chief change is seen in the intestinal mucosa, but there are present as well abundant signs of a widespread toxæmia in other organs of the body. At first the process consists of acute hyperæmia of the mucosa of the large intestine, which, should life be sufficiently prolonged, ends in colliquative necrosis of the mucosa with involvement of the last two feet of the ileum—though, rarely, the whole of the ileum and the greater part of the jejunum may be similarly affected.

It is not generally realized that the specific lesions are most developed in the lower part of the intestinal canal, especially the rectum and pelvic colon. On opening the abdomen a paralytic distension of the large intestine is often found; the mucosa is bright red in colour, very friable, and may actually drip with blood. Few, if any, intestinal contents will be found and the lumen may be occupied by viscid blood-stained mucus, or it may be pure blood and serous fluid. A general lymphoid peritonitis has been observed with the escape of free serum into the peritoneal cavity and the deposition of lymph flocculi on the peritoneal surface, together with œdema of the mesentery, especially at its posterior attachment. Post-mortem intussusception may occur. The mesenteric glands are inflamed and diffuse. The right side of the heart is engorged, the liver enlarged and congested with consequent parenchymatous changes. The gall bladder usually contains scanty and viscid amber-coloured bile. The spleen is generally dark, engorged and slightly diffluent, weighing about ten ounces. The suprarenal glands are congested and may show central necrosis.

In cases which do not run such a rapid course the intestinal mucosa is of plum-red colour, stippled with submucous hæmorrhages, and the whole gut wall infiltrated and œdematous. Should the patient survive a week or more, these inflammatory changes result in colliquative necrosis of the mucosa ; the mucous membrane is converted into an olive-green, or it may be blackish, substance, rigid to the touch, and often honeycombed in a peculiar manner ; this substance represents the dead and functionless mucous membrane and it is therefore incorrect to describe it as " diphtheritic " dysentery, a term used by German authors. Exceptionally, the whole bowel wall may be converted into such a gangrenous substance. The peculiar green tint which this necrotic mucosa assumes is thought to be due to staining of the defunct tissues by bile pigments.

The intestinal contents in these cases generally consist of a dark-grey fluid containing much altered blood without the addition of mucus, which cannot be secreted when once the destruction of the goblet cells has taken place. The colliquative necrosis may have a patchy distribution and may be confined to limited areas, as for instance, the hepatic and splenic flexures, or the descending and pelvic colons.

Should the patient survive, as he seldom does, such an extensive destruction of the bowel wall, the now defunct membrane is exfoliated in much the same manner as a diphtheritic membrane, exposing a raw, bleeding, granulated surface underneath. In a bowel which has undergone such disintegration complete regeneration of the mucosa does not take place ; restoration of the mucous membrane proceeds from islands of mucous membrane which escape unscathed. The whole process of repair would appear to constitute a struggle between proliferation of the specialized epithelium and fibrosis.

Chronic ulceration of the large bowel in bacillary dysentery takes place in varying degrees of severity. The smallest lesions consist of lenticular ulcerations of the mucous membrane, involving the mucosa alone ; the more advanced lesions consist of ulceration of limited tracts of the mucosa, rarely penetrating beneath the muscularis. That ulceration may, although very rarely, proceed to ante-mortem perforation appears to be beyond doubt. The ulcers are roughly ovoid in shape, and run transversely to the long axis of the gut.

The ulcers of bacillary dysentery may be distinguished from lesions in dysentery of amœbic origin by the fact that they commence on the free edge of the transverse folds and run transversely, not longitudinally, to the long axis. In shape they are irregular in outline, with ragged undermined edges, often intercommunicating with neighbouring ones in contradistinction to the oval and rather regular shaped, isolated amœbic ulcer. The intervening mucous membrane is hyperæmic, œdematous and plum-coloured and there is no compensatory thickening of the gut. In amœbic ulcers, on the other hand, the intervening mucous membrane is healthy and there is considerable hypertrophy of the gut wall.

Another pathological condition, which is the direct sequel of chronic bacillary dysentery, and has so far attracted little attention, is the presence of tapioca-like mucus-retention cysts, varying from microscopic proportions to the size of a cherry stone, which jut out on to the mucosa and are situated beneath the scars of old ulcers. These cysts become secondarily invaded by *B. coli* organisms and frequently a peculiar *B. coli* septicæmia results, leading to formation of pyæmic abscesses in the cortex of the kidneys and very often to a fatal termination. They appear to be formed as the result of an adenomatous downgrowth of Lieberkühn's follicles into the submucosa. Apparently in the formation of scar tissue part of the fundi of the crypts is nipped off.

Polypoid outgrowths reaching ¾ to 1 in. in length, scattered throughout the rectum, have been observed as the result of a chronic bacillary infection.

Typical dysentery bacilli can be isolated from the gut in all stages of the disease. When the mucous membrane is necrotic, it is necessary to remember that successful isolation depends upon procuring material from beneath the necrotic tissue, where alone the bacillus can be found ; for this purpose one should sear the tissue with a red-hot knife and then scrape it away. Failure to remember this results in the isolation of putrefactive organisms, such as *B. pyocyaneus*, which are found in necrotic tissue and which have nothing whatever to do with the pathogenesis of acute dysentery.

The bacillus has been recovered from the mesenteric glands, but never from the bile or blood post-mortem, though Flexner-Y organisms have been isolated from the blood-stream during life by Ledingham, Boyd, and others, and it is recorded that Wilson in France recovered the bacillus on three occasions by hæmoculture of 88 acute Shiga cases. He also obtained both organisms, Shiga three times, Flexner eight times, out of 1,113 urines cultured.

In the most acute stage the mucous membrane is infiltrated with lymphocytes and plasma cells, the capillaries are engorged and the submucosa is the seat of numerous capillary hæmorrhages. The goblet cells show signs of great secretory activity. The inflammatory changes are most intense in the lymphoid follicles.

In the necrotic stage the whole mucosa has undergone coagulation necrosis and is converted into a structureless layer, in which only polymorphonuclear leucocytes with disintegrated nuclei can with difficulty be distinguished. The submucosa is greatly thickened to twice or three times its normal dimensions owing to œdema and hæmorrhage. In fact, the chief feature would appear to be the destruction, or endothelial spoiling, of the nutrient vessels.

In the majority of microscopic sections of such an intestine, numbers of large macrophage cells, derived apparently from the endothelium of blood capillaries and lymphatics, may be distinguished. These cells are often of a considerable size, 15 to 20 microns in diameter, and may contain ingested leucocytes and red blood corpuscles. When voided in the stools they constitute a characteristic feature of the cellular exudate and, owing to their large size, refractility and phagocytic propensities, are apt to be mistaken for *Entamœba histolytica,* a point which will be referred to later.

Amongst Eastern peoples who are subject to recurrent attacks of bacillary dysentery, acute lesions are occasionally seen in a bowel which has recovered from a previous attack, with consequent scarring and fibrosis. The amount of destruction to which such a bowel may be subjected, compatible with life, has to be seen to be believed. Some of the large intestines of Turkish prisoners for instance resembled pieces of parchment with radiating fibrotic scars, the result of healed dysenteric ulcers.

Amœbic ulceration may be superimposed upon a healed bacillary dysentery, though it is more usual to find an acute bacillary process terminating the more chronic amœbic disease.

Symptoms.

The incubation period of bacillary dysentery is probably 2 to 7 days. The clinical symptoms are never so characteristic that the clinician can afford to neglect the advantages of a laboratory diagnosis, and there is no disease in which the mutual co-operation of the clinician and pathologist is so necessary. All degrees of severity may occur, from a mild diarrhœa of three days' duration with passage of blood and mucus in the stools, to fulminating cases with death supervening in the same period.

On clinical grounds, bacillary dysentery can be classified into five types (a) mild, (b) acute, (c) toxic or fulminating, (d) relapsing, and (e) chronic.

The fulminating type may be divided into two sub-groups—the choleraic and the gangrenous. The onset is acute, generally with vomiting; collapse with its attendant phenomena sets in early. The temperature is subnormal, the tongue dry and glazed, the skin cold and clammy, and the patient may complain of cramps. There is an initial watery diarrhœa, which is soon replaced by dark-red mucus containing a high proportion of blood or, it may be, serum alone. It is hardly necessary, from their superficial resemblance to cholera, to emphasize the importance of these cases.

The gangrenous form also commences suddenly with a rigor, headache and vomiting and other evidences of a severe toxæmia. The face is flushed; the pulse rapid and bounding. The abdominal pain and tenesmus are very severe, but as the toxæmia increases these wear off. This is a point in prognosis, and one should be suspicious of patients with pyrexia who become insensitive to abdominal pain; it is by no means a favourable omen. The stools at first resemble "meat-washings," but towards the end are composed of dark-grey offensive fluid, containing much altered blood. The underlying pathological cause of the absence of mucus is to be found in the total destruction of the goblet cells.

Important points to remember about the chronic form, which is more frequently seen in debilitated natives, are its intractability and the nature of the stools, which may show no external signs of blood or mucus for many months at a time. The great improbability, amounting sometimes to an impossibility, of isolating a dysentery bacillus from the fæces, though the organism may be present in the intestinal wall and can be found at autopsy, renders the diagnosis of these cases during life a matter of very great difficulty indeed.

Several complications occur in connection with bacillary dysentery. Of these arthritis is the most frequent; it generally affects one joint alone, but cases have been recorded in which both knees, wrist, fingers and even the temporo-mandibular joint have been involved. It is apparently quite common in some epidemics, and one small series of cases was observed in Egypt in which no less than 27 per cent. developed polyarthritis. The joint effusion is ushered in by pyrexia, rarely during the acute stages of the disease, more generally after the tenth day of the disease when the stools have once again become fæcal. The cases are usually Shiga infections, though Flexner cases have been recorded by Waller in Mesopotamia. The joint fluid is clear, never purulent, and is usually sterile on culture, though in one instance a culture of Shiga's bacillus was obtained from the joint fluid by Elworthy. Waller has recorded that it usually contains specific agglutinins for this organism. In the majority of cases the fluid is completely absorbed and no permanent injury to the joint remains, albeit convalescence may be considerably protracted.

General œdema was noted in Salonika in acute phases of some Shiga infections, in which there appeared to be a flooding of the tissues with dysentery toxins. In late stages also œdema was noted together with the development of ascites. No evidence of a coincident nephritis was obtained.

Conjunctivitis with pain, lachrymation and photophobia must now be regarded as due to the absorption of dysenteric toxins. It is liable to ensue from the 14th to the 34th day of the disease in convalescent cases and appears to have been specially common in Salonika. Iridocyclitis must also be regarded as a complication although a rare one. It bears no characteristic features and usually supervenes during convalescence. It is usually associated with arthritis.

Parotitis, either uni- or bilateral, may supervene, though it is by no means certain whether it can be regarded as a true complication.

Intussusception of the large intestine may occur, though it is more usually found in children.

Collapse may occur early in the illness from toxæmia, or later in the third or fourth week apparently from physical exhaustion and the draining of fluid from the body by continuous evacuations. The clinician should always be on his guard to forestall, if possible, this serious condition.

Neuritis of one or both legs following bacillary dysentery has been noted in chronic cases. It is doubtful whether the complication is to be ascribed to dysentery toxins or to an independent infection.

The sequelæ of bacillary dysentery may be the result of mechanical alterations to the bowel wall, or the direct effect of the absorption of toxins. In the former instance stenosis of the large intestine may occur leading to an obstinate post-dysenteric constipation with painful peristalsis and dyspeptic symptoms.

Tachycardia subsequent to bacillary dysentery was frequently observed in men in convalescent camps. It may be ascribed partly to the physical exhaustion this disease entails and partly to a toxic myocarditis. If neglected, or unrecognised, it may even lead to sudden cardiac failure.

Enright and Manson-Bahr have shown that invasion of the blood-stream by *Bacillus coli* is liable to take place through the chronic bacillary lesions, leading to formation of metastatic abscesses in the kidneys.

Prognosis.

The prognosis in bacillary dysentery depends very much upon the virulence of the particular epidemic, the age and physical condition of the patient. The infection appears to be specially virulent in those races, who for generations past have not been exposed to infection.

The prognosis is not good in cases with a subnormal temperature, rapid pulse, and a tendency to collapse ; while vomiting and persistent hiccough may be regarded as constituting almost invariably fatal signs. In the majority of cases, as regards expectation of life, the prognosis may be considered good, but it is otherwise as regards the permanent injury to the intestinal canal which this disease involves.

A series of 70 cases specially observed in France by Captain H. Letheby Tidy may be quoted here as probably typical of the usual disposal of the patients. The cases fell into three groups :

(1)	Evacuated to convalescent depot.	50=71 per cent.
(2)	,, ,, the United Kingdom	12=17 ,, ,,
(3)	Method of evacuation doubtful ..	8=12 ,, ,,

In the cases of the first group the average duration from onset to evacuation to a convalescent depot was 30 days, and the average duration of diarrhœa 8 days, leaving 22 days in hospital after cessation of diarrhœa before the men were fit for convalescent life. The factors which were found to be important in estimating such fitness were the condition of the bowels and the pulse.

A man was considered to have diarrhœa if he had more than two motions daily. Until diarrhœa in this sense had been absent for one week he was not fit for solid diet, and only if one week on solid diet produced no relapse of diarrhœa was he fit for the convalescent depot. Softness of the motions appeared to be of much less importance than their frequency. No cases were sent to the convalescent depot unless the stools had been negative for three consecutive examinations.

In some cases, usually in the fourth week, the pulse became rapid. When this occurred the patient needed a long convalescence.

The second group comprised all cases which had been classed as dangerous from their general symptoms, and all cases which on the 20th day from onset were still passing four stools daily. All such cases were found to need a long period of treatment and recovered very slowly.

From the military standpoint all cases of the disease, even if apparently mild, should be considered unfit for duty until a microscopic examination of the fæces shows an absence of any inflammatory cells or desquamated epithelium and until complete restoration of the digestive functions has been established.

Many clinically severe cases recover completely, while others continue to pass diarrhœic and dysenteric stools, it may be for several years after the initial attack; in these the destruction of the bowel tissue is progressive and they ultimately end fatally. Cases initially acute with persistent diarrhœa should no longer be considered fit for active service. Those with chronic ulceration of the bowel and continuous passage of mucopurulent stools are most intractable and distressing and should therefore be regarded as entitled to permanent pensions.

It is questionable how far the mucosa can regenerate after such a severe destruction, but undoubtedly many cases, especially in the young and vigorous, completely recover and should be judged upon their general condition. In contradistinction to the amœbic form, bacillary dysentery is not prone to relapse and need not necessarily be pensionable. But it should be borne in mind that a previous bacillary ulceration undoubtedly predisposes to the development of amœbic colitis. Cases of this nature are being frequently encountered among pensioners who suffered undoubtedly from bacillary dysentery in the first instance, but whose subsequent relapses were due to infection with the *Entamœba histolytica.*

Bacillary dysentery when complicated with other specific fevers is a dangerous combination; in Gallipoli it co-existed frequently with paratyphoid fevers and it may be mentioned that subtertian malaria together with bacillary dysentery generally assumes a grave aspect and requires a most vigorous and thorough antimalarial treatment. A grave prognosis should also be given in cases complicated with lobar or bronchopneumonia.

The average duration of invalidism from dysentery may be gathered from the following tables. In the first, compiled from index cards and admission and discharge books by the Medical Research Council, a series of 3,000 cases of dysentery has been taken from the records of patients treated in military hospitals in France and Gallipoli in 1915, and includes cases both of brief and of long duration. The second table shews a series of 2,000 cases from France, Salonika, and Egypt during 1917 and 1918, taken from the records of cases treated to a conclusion in the special convalescent depot for dysentery at Barton-on-Sea.

Cases of Dysentery in 1915.

Force from which derived.	No. of Cases.	Total No. of Days under Treatment.	Average No. of Days under Treatment.
France	681	28,823	42·3
Gallipoli	2,319	175,365	75·6
Total	3,000	204,188	68·1

Cases of Dysentery in 1917—1918.

Force from which derived.	No. of Cases.	Total No. of Days under Treatment.	Average No. of Days under Treatment.
France	1,586	187,666	118·3
Salonika	330	82,672	250·5
Egypt	84	12,018	143·1
Total	2,000	282,356	141·2

The various forms of dysentery have not been differentiated.

Diagnosis.

Though acute dysentery, occurring in epidemic form in armies in the field, may be justifiably regarded as bacillary dysentery, yet it is always advisable to resort to laboratory diagnosis whenever possible. It was found, however, even in France, where the facilities for scientific work were probably greater than in any other of the theatres of war, that it was quite impossible for bacteriological examination to be applied to all cases admitted to casualty clearing stations. It was accordingly ordered that cases, in which the passage of blood and mucus was observed, should be diagnosed as "clinical dysentery," and that the bacteriologist's labours should be directed first to the cases in which these symptoms were not established. This examination presented many difficulties to the uninitiated. In order to economize in men and material it was advisable to employ as pathologists those who had been especially trained in this branch of work, for besides a knowledge of bacteriology, a considerable insight into cellular pathology and an intimate acquaintance with the varied protozoological fauna of the intestine are required.

The gross character of the stools passed during different stages of the disease varies considerably and certain rules may be laid down for the guidance of the military clinician, though it must be admitted that exceptions occur. The acute bacillary stool consists of pure blood and mucus, or more accurately "bloody mucus." It is in fact mucus tinged with bright red blood, of extreme viscosity, and tending to adhere to the bottom of the bed-pan or containing vessel. It is odourless or bears a faint smell of spermin. It represents, in fact, an acute inflammatory exudate, derived from the mucosa of the whole or major part of the large intestine. The amœbic stool, from which it is necessary to differentiate it, is composed of blood and fæces intimately mingled, is very offensive, not viscid, and represents the exudate and sloughs derived from ulcers throughout the canal, the dark altered blood being derived from small intermittent hæmorrhages at the bases of these ulcers.

The diagnosis of bacillary dysentery can be made sufficiently accurate for all practical purposes by examination of the cellular exudate alone. In military practice what is most required is promptness; it is necessary to diagnose early in order to save the patient's life. The clinician in a casualty clearing station cannot afford to wait twenty-four hours before applying the appropriate remedy. If a few hours' delay takes place, it may result in irreparable damage to the gut wall, and one cannot restore a once scarred and fibrosed intestine.

A provisional laboratory diagnosis may be made by direct examination of the cellular exudate under the microscope, by recognition of the predominant type of cell and by exclusion of the *Entamœba histolytica*. As seen under the one-sixth lens the characteristic cellular picture is one composed for the most part of undamaged polymorphonuclear leucocytes. They constitute over 90 per cent. of all the cells in the exudate. Willmore and Shearman have noted that the ringing of the nuclei of these cells is specially distinctive. The large macrophage cells, which, as previously mentioned, are derived from the submucosa, constitute about 2 per cent. of the cells and are present in the mucus, especially in the early stages of the disease. They are large hyaline cells 20-30 microns in diameter; sometimes they are round, oval or even bi-lobed in outline and in their protoplasm they contain vacuoles and fatty globules of various shapes and even ingested red cells or leucocytes. The pathologist should make himself familiar with these cells as they are extremely liable to be mistaken for *Entamœba histolytica* and consequently lead to a mistaken diagnosis.

The following are the points which require attention, in order to avoid those mistakes in diagnosis which frequently occurred. In bacillary dysentery the macrophage cells are defunct and consequently non-motile ; they are by no means as refractile as is the *Entamœba histolytica* and their protoplasm has a bluish ground glass appearance. The characteristic endothelial nucleus can seldom be made out as it is usually undergoing chromatolysis. Columnar epithelial cells are frequently present with the macrophage cells and, in the later stages of the disease, intestinal protozoa such as *Entamœba coli* and intestinal flagellates (*Trichomonas* and *Chilomastix*) may make their appearance. The *Entamœba coli* is specially liable to cause a fallacy in diagnosis, for, unless the pathologist is familiar with the morphological characters of the non-pathogenic amœbæ, a mistaken diagnosis, or even a suspicion of a double infection with the two main forms of dysentery, may arise.

For successful laboratory diagnosis it is essential that the stool should be fresh and passed early in the course of the disease.* It should, if possible, be collected in a bed-pan without admixture of urine and brought straight to the laboratory. On no account should the selection of a portion of the stool suitable for examination be left to an attendant or orderly, for it may happen that an unsuitable portion may be chosen and unnecessary delay thereby caused. The dysentery bacilli are delicate and soon become overgrown by more hardy saphrophytic organisms ; in hot climates this decomposition takes place very rapidly, usually in a period of four to six hours. A better method, wherever it can be arranged, is for the pathologist himself to obtain a portion of blood and mucus direct from the patient by means of a rectal swab.

Dysentery bacilli, especially Shiga's bacillus, grow less vigorously than other intestinal organisms and their growth may be easily inhibited by the employment of dyes or inhibiting agents. Probably the best medium for the purpose is litmus-agar containing 1 per cent. of lactose, though MacConkey's medium is widely used and gives satisfactory results. A small portion of blood and mucus which, if contaminated with fæces, should be first washed in sterile water or saline, is spread upon the dried surface of the plate in a spiral manner.

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* The statistics of Martin and Williams show that, out of 1,050 efforts to recover the dysentery bacillus at various periods of the disease, 68 per cent. of positive results were obtained in the first five days, 17·4 per cent. in the second five days, and 6·3 per cent. in the third five days.

One need not be too sparing with the amount used, and no attempt should be made to incubate the mucus in ordinary bile broth preliminary to plating. The plate should be examined by means of a watchmaker's lens after 24 or preferably after 48 hours, as the dysentery colonies become more obvious after prolonged incubation. They are transparent, of a small size and bluish colour. They generally occur in irregular chains interspersed between other more vigorous organisms. Considerable experience is necessary before one becomes so familiar with their appearance as to be able to differentiate them from those of *B. fæcalis alkaligenes* and the intestinal streptococci.

For rapid identification of the bacilli under active service conditions it suffices to pick off a certain number of colonies by means of a platinum spud and, after making a dense emulsion in a small quantity of saline, to place them with drops of specific Shiga and Flexner-Y sera, in suitable dilutions, upon a Garrow's agglutinometer. On this instrument macroscopic agglutination takes place within five minutes, and is therefore of considerable practical importance. Should marked agglutination in one or other serum take place, subculture should be made on to agar, to be subsequently confirmed by sugar reactions.

For more complete diagnosis subcultures should be made direct from the colonies on to agar, the organism stained by Gram and tested for absence of motility. Subcultures should be planted out on to four sugar media, viz., glucose, lactose, mannite, and dulcite, and the reactions recorded after 24 hours' incubation at 37°C. The results obtained should be confirmed by agglutination, for which suitable polyvalent sera, embracing if possible the five chief types of Flexner-Y, are necessary, together with a Shiga serum. The macroscopic method must be resorted to, the microscopic being fallacious. Progressive dilutions of specific serum should be made in tubes until a titre of 1 : 2000 is reached, to which opalescent emulsions of the organisms should be added. It should be remembered that dysentery bacilli do not agglutinate readily, so that the time allowed should be at least four hours at 50°C. in a water bath, and precipitation should be permitted to occur at the air temperature for which an additional 10 to 12 hours should be allowed.

A reliable emulsion can be made from a 24-hour broth culture to which 0·1 per cent. formalin has been added. Paragglutination may occur by this means, so that it is best to neglect results not attaining to a quarter of the full titre of the serum.

Serodiagnosis is a method of diagnosis applicable only to convalescent cases; it is obviously unsuited to acute cases in whose blood agglutinins have not yet formed. In skilled hands, however, it has proved its value. Dreyer's technique should be employed, on account of the standardization of the emulsions, and according to Martin gives useful information in about 50 per cent. of cases. In the case of Shiga dysentery, provided that ultra-sensitive strains are not used, the diagnosis is consistent, but in the case of Flexner-Y dysentery the results have been less encouraging, possibly because a sufficiently wide range of agglutinable emulsions has not so far been available. These emulsions should now consist of the five serological races of Andrewes and Inman, comprising the V, W, X, Z, and the Y bacillus of Hiss and Russell. It is obvious that the employment of so many emulsions must render this method of diagnosis a very laborious one, and therefore unsuited to routine use in times of pressure. The general opinion appears to be that in Shiga infections a positive diagnosis can be established by agglutination occurring in a dilution of 1:25; but in the case of the Flexner-Y group it it necessary that agglutination should occur in a considerably higher titre, at least 1:50. In making such a diagnosis the possibility of the patient having suffered from an attack of dysentery previous to the one under consideration, and the possible effect of inoculation with dysentery vaccine, must be taken into account.

Treatment.

With regard to treatment, should bacillary dysentery be brought under treatment at an early stage of the disease, a cure is a matter of no very great difficulty; this is especially true of the more acute types of the disease. In war, however, it is obvious that this cannot always be done, and, therefore, under these conditions a certain amount of destruction of the mucous membrane has already taken place before an opportunity for efficient treatment is secured.

The main principles consist in placing the patient so that his intestinal canal is at rest and the diet he absorbs is as nutritious as possible, with the least amount of non-absorbable residue.

Fulminating cases require the most vigorous measures, and the methods adopted may be applied with modifications to the less acute clinical forms.

If collapse is imminent it is best to keep the patient warm with hot water bottles. When the passage of stools is almost continuous the patient should on no account be permitted to exhaust his strength by straining on a bed-pan; it is much better in these cases to pack him well with tow or cotton wool on a waterproof sheet, which can be changed every few minutes. It is most necessary to forestall, if possible, the advent of collapse, for when once this condition has been fully established it is too late to restore the patient. Intravenous injections of normal saline should be generously given, up to two or three pints. Even more has been advocated. The injection of smaller quantities is followed by a temporary improvement only. To the saline solution may be added atropine, gr. $\frac{1}{100}$ in 1 pint of water. Good effects have been obtained by intravenous injection of Rogers' hypertonic saline (sod. chlor., grs. 120, calc. chlor., grs. 4, pot. chlor., grs. 6, water, 1 pint, to which may be added glucose, grs. 35). This solution should be given slowly, and at a temperature of 104° F.

It is customary to commence treatment by a preliminary purge in order to clear the large intestine of any remaining fæcal contents; the best for this purpose is $\frac{1}{2}$-ounce of castor oil containing about 15 minims of tinct. opii. The following morning routine treatment with saline aperients should be commenced. The best salt is the sodium sulphate, which should be given in drachm doses every two hours for the first twenty-four; thereafter, every four hours until the stools become fæculent. The routine use of opium in the treatment of bacillary dysentery cannot be too strongly deprecated. Its main uses are to procure rest and sleep, or to enable a patient to stand a long journey as, for instance, evacuation from a field ambulance, but it should on no account be regarded as a means of curing the disease.

Tenesmus and dysuria are best relieved by a cocaine suppository; if excessive, a morphia injection is permissible.

The routine use of bismuth has many adherents, but it has little result save to clog up the bowel, which should be kept clear of contents as much as possible.

In Central Europe, *bolus alba-kaolin*, with the addition of animal charcoal in doses of three tablespoonfuls of each, is used. It is said to check excessive diarrhœa and to act as an intestinal antiseptic.

Intestinal antiseptics, such as salol or cyllin, do not appear to have much effect in the acute, though they have their uses in the chronic forms.

Treatment by anti-dysenteric serum has been employed, and diverse opinions have been expressed regarding its value. The serum which is placed on the market is a polyvalent one, and, as pointed out by Dudgeon, its chief deficiency is in anti-Shiga immune bodies. If it were possible to obtain a greater degree of anti-bacterial power towards Shiga's bacillus than is at present the case, the diversity of opinion which exists would probably soon disappear. In the future it may be more advantageous to issue a Shiga monovalent serum to field medical units, since the Shiga infections are clinically the most severe and therefore the most likely to require this form of treatment. The main point with reference to anti-serum is that it should be given early, if possible during the first five days, and in sufficient quantities. Bacillary dysentery has many points in common with diphtheria, and the action of anti-dysenteric serum may perhaps be regarded as analagous to that of anti-diphtheritic serum. Once the mucous membrane of the gut has become necrotic, it is doubtful whether the serum has any effect at all. It is obvious, therefore, that a field medical unit, and not a base hospital, is the proper place in which to administer it.

In very acute cases, the intravenous route, in doses of 60 c.c., is the most efficacious. The next most efficacious method is the intramuscular route ; this proved to be a most convenient method. A large amount of serum up to 120 c.c. can be injected with the minimum of pain into the adductor muscles of the thigh, where the intramuscular planes will accommodate large quantities. When it is necessary to give a very large dose, half the amount may be given into each side, care being taken to avoid the femoral artery. This is a much less painful method than injecting into the flanks or superficial tissues of the abdomen, and a more efficacious one.

There is a danger—a very remote one, it is true—of anaphylactic shock supervening, especially after intravenous injection. This most alarming phenomenon has, however, occurred, although two cases noted by Manson-Bahr were not fatal. Before giving an intravenous injection of any magnitude, it would be well to enquire whether a dose of serum has been given some time previously. It is generally advised that an attempt should be made to desensitize all previously serum-treated patients by a preliminary injection of a small dose (2 c.c.) of serum six hours or so before the main dose is given.

A certain mild reaction is apt to follow the injection of serum. It has been noted that, on the day following, even an exacerbation of the symptoms may take place, but these soon abate. Should toxæmic symptoms still persist, injections of the serum should be repeated at an interval of three days.

Improvements in the method of storage of serum under active service conditions are required. In future it would be preferable to employ a strong anti-Shiga serum alone for severe cases, as these are generally infected with that organism, and it would be advisable to stock it in large phials of at least 25 c.c. capacity each, in a more suitable form for massive dosage. Serum sickness is apt to supervene six to ten days after the injection; this is specially the case when long-stored serum is used. It cannot be sufficiently impressed upon officers in charge of base medical stores that all sera should be kept on ice, and stocks in the field should be frequently renewed.

Statistics on the value of serum treatment are notably difficult to compile or adjudge; but on the whole, the opinion of the majority of clinicians during the war has been favourable, though some consider that it predisposes to the development of arthritis. The latest figures given by Klein from France and Waller from Mesopotamia show that if given early in doses of 120 c.c., and preferably intravenously, it considerably diminishes the death rate and hastens recovery.

It is quite unnecessary to regard milk as the one and only diet in intestinal disease; as a matter of experience, plain milk, whether boiled or unsterilized, is badly borne by severe cases of bacillary dysentery, besides being unpalatable and monotonous. The casein is passed quite undigested, and appears as clots in the stool. The ideal diet should be un-irritating, easily digestible, and should be as valuable as possible from a nutritive point of view. The best method is to give small feeds every two and a half-hours, consisting of tea, albumen-water, jellies, bovril, Brand's essence of chicken tea in six to ten ounce doses. The introduction of solids into the diet too soon may lead to sudden collapse, or to a profuse diarrhœa in a case which is doing well. On the other hand, it is unnecessary to go to the other extreme and adhere to a too rigid diet of albumen-water for a week or more at a time. Useful additions to the diet are boiled arrowroot, cornflour shape and stewed fruit. A return to a meat diet should be made very gradually. This important point must be emphasized in convalescent depôts, where special arrangements for dieting convalescent dysenterics must be made. A return to a tinned beef diet should on no account be attempted till an interval of at least six weeks has elapsed from the initial attack.

As regards local treatment, the mouth should be kept clean. The abdominal pain is best relieved by hot water bottles or turpentine stupes. Vomiting and hiccough should both be regarded as symptoms of serious import. A patient in whom the latter symptom makes its appearance is not likely to recover.

The treatment of the less acute cases should, more or less, follow the lines already laid down, but it is probably unnecessary for all to receive serum treatment. The indications for the administration of anti-serum are the presence of signs of toxic absorption, the number of the stools exceeding 18 in the 24 hours, and a remittent pyrexia, a rapid pulse, and great abdominal pain.

The treatment of chronic bacillary dysentery is at the best unsatisfactory, and taxes all the resources and ingenuity of the physician. The course of treatment usually advocated is rectal lavage, for which protargol, 0·5 to 1 per cent. is considered most preferable ; recent experience shows that freshly prepared eusol may be used with benefit. A well-lubricated stout rectal tube should be inserted, and solutions given by means of a funnel by gravitation, the patient being in the knee elbow position. Rectal lavage should be combined with abdominal massage, and small doses of salts given by the mouth.

Vaccine treatment has been disappointing. In East Africa a mixed vaccine of Morgan's, Shiga's and Flexner bacilli, 750, 250, and 500 millions per c.c. respectively of each, was used in doses of 2, 4 and 8 c.c. at intervals of a week. It is possible that the failure is due to non-administration of a homologous vaccine. It would be advisable, whenever possible, to make a vaccine from an organism isolated from the patient's own stools.

The surgical treatment of chronic bacillary dysentery by means of appendicostomy has so far not proved to be satisfactory, but possibly with modifications and improvements in the fluid used for lavage it may be useful in alleviating this most distressing condition.

More recently, however, cæcostomy and the insertion of a Paul's tube with the formation of an artificial anus in the right iliac fossa has proved more satisfactory. By this means the large bowel may be placed at rest for a period of three months, and the opening then closed.

With regard to complications, dysenteric arthritis is best treated by back splints, application of Scott's dressing, hot air treatment and massage. Should the joint cavity be greatly distended, aspiration with aseptic precautions will temporarily relieve the pressure.

Conjunctivitis and iritis are best treated by atropine drops and the application of an eyeshade.

When malaria, especially of the subtertian variety, is the primary infection, the case should be treated primarily from the malarial point of view, that is to say, quinine had best be given in 12-grain doses on three successive days by the intramuscular route; in cases of benign tertian malaria, should the patient be capable of retaining it, quinine solution by the mouth will suffice. Anti-dysenteric serum in sufficient dosage should be injected at the same time as the quinine is administered.

Prevention.

With regard to preventive measures, the spread of bacillary dysentery from one man to another may take place by direct contact, or through fæcal contamination of utensils, dishes or food. But this can only take place when the most elementary rules of sanitation are neglected. As in all other cases of intestinal diseases, the prevention of bacillary dysentery in armies and in camps is directly dependent upon the method of sanitation.

There can be little doubt that the disease is spread by the presence of actual carriers of the disease. From a military point of view it is most important to detect and control all such individuals, but it is doubtful whether, with the laboratory means at one's disposal and on account of the labour involved, this really can be done. From the various investigations made by Fletcher, Doris Mackinnon, Lepper and Perry, persistent carriers of dysentery bacilli, that is, individuals who continue to excrete dysentery bacilli longer than three months after the beginning of the illness, occur quite commonly, forming about 6 per cent. of dysentery convalescents. Carriers of the Flexner-Y bacillus appear to be four times as common as are Shiga carriers. The excretion of the bacillus appears to be very intermittent; thus Fletcher records the discovery of the bacillus on the third and even the fourth attempt. The carrier state diminishes with time, and most individuals are free from infection after the ninth month subsequent to recovery. According to Perry, chronic carriers of both infections have been found to exist; in Shiga cases they constitute 4 per cent. and Flexner cases 7 per cent. of total convalescents. With a view to ascertaining when a carrier becomes free from infection, a large amount of labour is necessary; according to Fletcher stools should be examined daily until the results are negative for a period of four weeks. The average Flexner-Y carrier is generally in good health; his motions may be formed, and he is fit to undertake work, unless subjected to very adverse conditions. On the other hand, the Shiga carrier is generally an invalid; his stools contain blood and mucus and he is subject to frequent attacks of diarrhœa. The bacilli are present only in the mucus and not in the fæcal matter, so that the presence of mucus in the stool of a convalescent dysentery patient should be appreciated at its true value and no case discharged from hospital in this condition. For the same reason in military practice it is necessary for medical officers to detect and, if possible, evacuate mild or early cases of bacillary dysentery directly they report sick; such cases probably constitute one of the most important factors in the spread of epidemics. In practice, it is advisable to place bacillary cases, in so far as is possible, in wards by themselves; the spread of the infection in hospital, especially to surgical cases, has been frequently observed and every effort should be made to prevent this.

The transmission of bacillary dysentery by the agency of house-flies is undoubted. They play a very important part in its spread, and it is a matter of common knowledge that epidemics of bacillary dysentery generally coincide with the maximum prevalence of these pests. This was certainly the case in Gallipoli in 1915, and proved to be the same in Salonika, Egypt, Palestine and Mesopotamia. Buxton's figures from the last-named theatre of war show that 63 per cent. of flies caught in a British camp had human fæces in their intestinal canal. The actual isolation of the Shiga bacillus from the intestinal tract of flies caught in the open was first effected by Manson-Bahr in 1910, and it was proved that, under experimental conditions, dysentery bacilli can survive in the intestinal tract of that insect for at least five days; these results have been in the main confirmed by Taylor in Salonika. Measures directed against the spread of dysentery must therefore necessarily include those especially directed against the house-fly. It is difficult to understand how the house-fly manages to obtain so great a concentration of Shiga bacilli in its intestinal canal as to enable them to be isolated on culture. The dysentery organism is very susceptible to sunlight and is rapidly killed off in the open desert, and the supposition is that flies feed upon dysenteric fæces when freshly passed. It is all the more surprising to find that the organism can be obtained from the intestine of flies captured many miles away from human habitation; this, however, Manson-Bahr succeeded in doing in the Sinai desert in 1917. It therefore seems that some more intimate connection between the house-fly and the dysentery bacillus exists than at first sight appears to be the case.

With regard to the contamination of water by dysentery organisms, experiments upon the vitality of the organisms have led to the conclusion that Shiga's bacillus can survive and multiply in stored water for three weeks or more, especially at medium or low temperature, but cannot exist such a long time when exposed to the sun or when associated with large numbers of putrefactive micro-organisms. According to some observers, polluted water was responsible for the frequency and virulence of bacillary dysentery among the transport drivers in East Africa, and to a minor extent among troops in France during the later stages of the war. When all the drinking water is chlorinated, it is difficult to see what part water can play, though a false sense of security may be engendered by the belief that water, once chlorinated or sterilized, will remain so indefinitely. Dudgeon has shown that when once the effect of chlorination has worn off, water may become subsequently infected. Hence water once chlorinated must be efficiently protected from dust and flies.

As regards the spread of dysentery by dust, it was shown in France that dysentery organisms could survive for a considerable period in dust, if protected from sunlight, and it has been suggested that in temperate climates they may be disseminated by means of powdered fæces, but there is by no means conclusive proof that this does really take place.

Prophylactive inoculation against bacillary dysentery had until recently fallen into disfavour, mainly on account of the very severe local reaction which Shiga's bacillus produces. Graeme Gibson introduced a method of inoculation whereby the toxins of this bacillus were neutralized by a sufficiency of anti-Shiga serum, a procedure which considerably modifies the reaction. The vaccine and the serum are put up in twin phials, the bacillary emulsion being contained in one, the serum in the other. The first dose given is 0·25 c.c. containing 500 million Shiga organisms mixed with 0·1 c.c. of serum; the second dose, given ten days later, is 0·5 c.c. containing 1,000 million organisms with 0·2 c.c. of serum. The local reaction results in a painful inflammatory lump, though constitutional symptoms are absent. Gibson published a limited number of statistics in which the results appear to be favourable, and although this inoculation was largely used in France during the later stages of the war, it is still too early to make any general statement on the subject. The duration of the immunity conferred is not certain, though agglutinins can still be demonstrated in the serum after three months. A somewhat similar method was used in Germany and Austria during the war under the name of Boehncke's "Dysbakta."

As an accessory measure it may be mentioned that the provision of a certain amount of oil in the diet may probably constitute a defensive measure as calculated to lessen the amount of intestinal irritation predisposing to bacillary dysentery produced by sand and an unsuitable dietary.

Details of the measures adopted in France and England for the segregation of dysentery patients may be usefully repeated. In 1916 the orders in France were that all cases of suspected dysentery were to be sent to field medical units set apart for infectious diseases, certain clearing stations being detailed for this purpose, and at least two bacteriological and protozoological examinations of the dejecta were to be made. If the results were positive the patient when convalescent was sent to England through hospitals at the base, and, if the results were negative, to a convalescent depot in France. In the latter case if after seven days' interval a final examination in the laboratory again proved negative, the patient when fully recovered was to be discharged to his base depot, but in each case the man's unit was to be informed that he had been suspected of dysentery, and must not be employed on food or water duties.

In 1917 owing to a severe outbreak in a new division in the front line, orders were issued to the effect that all cases in the division which were suffering from diarrhœa were to be sent to a field ambulance for segregation and treatment. Any cases in field ambulances which showed blood and mucus in the stools, or were of any severity, were sent on at once to a selected casualty clearing station and dealt with as suspected dysentery.

In one army the general plan was adopted of watching for diarrhœa cases, separating them at the earliest possible moment, and treating them as possible dysentery cases. In Etaples a similar plan was adopted for the temporary segregation of any diarrhœa case.

These measures were subsequently made general throughout the forces on the Western Front in 1918.

In 1917 it was decided, in order to avoid needless evacuation to England, that mild cases of dysentery admitted to base hospitals who were fit to convalesce in France, estimated at 70–80 per cent. of the total admissions, should be sent either under special regulations to ordinary convalescent depots, or to special dysentery convalescent depots.

In June 1918 certain casualty clearing stations were detailed as dysentery centres. The following order was then issued:—"So far as the military situation permits, cases of diarrhœa, except those of a trivial nature, will be at once sent from their units to field ambulances for observation and treatment, and cases suspected to be dysenteric will be evacuated without delay from the field ambulance to the dysentery centre. To ensure that the milder cases of diarrhœa, retained for treatment in field ambulances, are free from dysentery, rectal swabs should be taken and sent by the most expeditious means to the dysentery centre for bacteriological examination. Field ambulances will obtain rectal swabs from the nearest mobile laboratory as required.

" Suspicious cases, in which the stools contain muco-pus or blood and mucus, will be diagnosed " dysentery " whether the bacteriological examination is positive or not. Where large numbers of cases are occurring, bacteriological effort will be especially directed to the cases which are clinically uncertain, typical cases being diagnosed on clinical grounds alone.

" Severe or protracted cases will be evacuated to the base, and as far as possible will be kept together on ambulance trains.

" Where the military situation permits, slight cases may be retained for treatment at dysentery centres and, when fit, discharged for duty, provided that, on return to ordinary diet and exercise, dysentery symptoms do not recur and that *three pathological examinations after the stools have become solid* exclude the presence of dysentery bacilli or amœbæ. When such cases are discharged, notification will be sent, in every instance, to the man's unit, stating that he has been under treatment at a dysentery centre, and that he must not be employed in the cooking or handling of food or on water duties."

During the summer of 1918 a large number of dysentery cases were admitted to the Boulogne base from all parts of the fighting areas. These coincided with a heavy influx of other casualties from wounds and mustard-gas poisoning, and it was extremely difficult to arrange special hospital accommodation so as to retain in France the lighter cases of dysentery during the relatively long period of special invalid dietary and general care which were necessary on clinical grounds in order to prevent the recurrence of intestinal irritation and relapse into a state of chronic dysentery.

Special centres were, however, established at No. 14 Stationary Hospital and at No. 7 Convalescent Depot. Patients who had suffered from a severe clinical attack, or had had a persistently positive laboratory report, were evacuated as soon as possible to England. The special hospital none the less soon became overcrowded with milder cases, and relief was obtained by early transference of them to the convalescent depot after one negative examination of the dejecta. No men were discharged from the depot until a total of three laboratory examinations had been made with negative results.

In the convalescent depot, which admitted casualties of all kinds, an area was marked off as a " Dysentery Isolation Area." In this area the patients had separate eating, sleeping and latrine accommodation. They wore hospital clothing as a mark of distinction at all times, and were then permitted to attend physical drill and all recreations in common with other patients in the depot, but not the general canteens. The medical officers had power to order special invalid dietary for those who presented evidence of persistent abdominal pain or of abnormal stools. When a man was considered fit for discharge to duty a final laboratory examination of the dejecta was made. If the report was negative, discharge was accompanied by the usual notification to the man's unit, sent through the base depot, to the effect that he had been treated for dysentery and should not be employed in connection with the preparation and distribution of food or purification of water supplies.

In England in 1916 a dysentery depot was established, to which convalescents were transferred from central hospitals. At the central hospital, the patient admitted from overseas was to be retained 14 days, and two laboratory examinations, bacteriological and protozoological, were made with an interval of seven days between them. If these examinations were negative and the patient required no active treatment, was on full diet with normal stools, and was fit to live in a hutted camp and to be drilled and exercised, he might be transferred to the dysentery depot. The reports of the laboratory examinations were at the same time to be sent to the depot. There he was to complete two clear months' convalescence from the time when he was first put on full diet and passed normal stools. Laboratory examinations were to be repeated. He might then be discharged to duty as from an ordinary hospital, but the unit was to be notified of the fact that he came from a dysentery depot. A notification was also to be sent to the medical officer of health of the district to which the patient went on furlough, and, when he proceeded overseas, a notification that he had suffered from dysentery was to be sent to general headquarters of the expeditionary force.*

In 1917 the special control of the dysentery cases transferred to England from an expeditionary force was strengthened by a fresh order† directing that all such patients should be sent to certain selected hospitals. From these hospitals, after two negative laboratory reports over a similar period of 14 days, and when the patient satisfied the same conditions, he was transferred to the dysentery convalescent depot at Barton-on-Sea. A third negative laboratory report, on an examination made three weeks after the last negative result or after the termination of specific treatment, justified the discharge to duty of a man otherwise fit, the form reporting his discharge being stamped with a warning that the patient was a convalescent from dysentery.

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* A.C.I. 1,354 of 1916.

† A.C.I. 205, dated 3rd February, 1917.

AMŒBIC DYSENTERY

The term amœbiasis denotes an infection with *Entamœba histolytica*, a protozoon primarily causing ulceration of the intestinal canal, but which by invading the bloodstream is liable to form metastatic abscesses in other regions of the body, mainly the liver. When the disease is confined to the intestinal tract it produces amœbic colitis or amœbic dysentery, of which the most frequent complication is amœbic abscess of the liver.

Amœbic dysentery, as compared with the bacillary disease, is insidious in its onset, chronic in its course, and very liable to relapse. The appearance of the lesions in the intestines is characteristic and easily differentiated from the acute inflammatory lesions of bacillary dysentery. Formerly considered to be confined to the tropics and sub-tropics, it is now known to be widely spread throughout the temperate parts of Europe, and during recent years indigenous cases have been reported from England and France. Persistent carriers of the cysts of the parasite, *E. histolytica*, are quite common, and the spread of the disease is due to the presence of this form of the parasite in their fæces.

Distribution and Ætiology.

The prevalence of amœbic dysentery amongst the various expeditionary forces, especially in Salonika, Egypt and Mesopotamia, has been extensively investigated. Investigations of this nature, however, have to be carried out by protozoological and bacteriological experts working conjointly, as the sources of error and fallacy are many.

Before going into this question, certain generalizations are permissible. Bacillary dysentery is a disease of soldiers under conditions of active warfare, in closely crowded camps, and on the march, while the more chronic, relapsing amœbic form is much more evident in convalescents at the base, men whose symptoms were not sufficiently obvious in the field to require extensive bacteriological investigation; therefore the ratio of amœbic to bacillary dysentery, as recorded by pathologists, will necessarily be higher in base laboratories than that obtained nearer to the seat of active operations. Add to this the facts that amœbic ulceration of the gut may exist for some considerable time without causing any symptoms, and that amœbic infection frequently supervenes in those who previously suffered from the bacillary disease, and it will then be readily understood that amœbic dysentery assumes its main importance in military medicine as the aftermath of war. This is certainly the case amongst pensioned men. The difficulties attending the bacteriological diagnosis of the more acute bacillary disease, so important in the field, have already been alluded to ; moreover, one should remember that bacillary dysentery can only be diagnosed with certainty during the earlier stages, and therefore cases have either completely recovered or are undiagnosable, bacteriologically speaking, on reaching the base. Amœbic dysentery, on the other hand, on account of its chronicity and liability to relapse, is more easily recognized.

It may be said that, taking a general view of the war as a whole, amœbic dysentery formed about 7 per cent. of all clinical dysenteries in the Eastern theatres of war, while in France and Flanders it played a very minor part. The official figures return it as 2·8 per cent. for these latter. Although it is recognized that this figure includes a number of relapses, yet a certain number of indigenous cases have been observed by French and British investigators. A point to be noted is that amœbic dysentery occurs at all seasons of the year ; whereas bacillary dysentery has a definite seasonal incidence, a fact which indicates the probability of the transmission of the former form of dysentery by polluted water, and of the latter by flies.

Available figures indicate that amœbic dysentery was not so common in Salonika as elsewhere in the East. According to Graham and Ramsbottom it is probable that only about 3 per cent. of the cases of dysentery there were of the amœbic type. The accounts given by Delille, Paisseau and Lemaire on the French side, and Dudgeon on the British, also seem to indicate that it played a minor part. In Gallipoli, unfortunately, exact figures are not forthcoming, but it is estimated that amœbic dysentery accounted for 10 per cent. of the total dysentery admissions.* In Egypt and Palestine, amongst British troops the amœbic rate varied from 2 per cent. of all dysenteries in 1916 to 7 per cent. in 1917 and 1918, according to Gunn, Savage, Woodcock and Manson-Bahr, while amongst Indian troops it was almost invariably higher, according to Woodcock as much as 15·7 per cent. In the latter part of the campaign the Palestine figures showed an even incidence of 7 per cent.

As might be expected from the climatic conditions, and the more intimate contact with Indian troops and native carriers of the disease, the amœbic incidence was certainly at its highest in Mesopotamia, as pointed out by Ledingham, Boney, Crossman and Boulenger. In the forward areas in that country the bacillary disease predominated, but amœbic dysentery accounted for 20 per cent. of acute dysenteries amongst British troops, while amongst Indian troops the rate of incidence was almost double. In the base area, on the other hand, the ratio of amœbic infections amongst British troops was very much higher, amounting to 40 per cent. at Basra.

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* For many reasons the statements of Bartlett (Quarterly Journal of Medicine, Vol. X. p. 185) that "at least 79·4 per cent. of the clinical dysenteries from Gallipoli had amœbiasis," and the results of his post-mortem findings that 91·8 per cent. of the bodies had amœbic lesions, have to be discounted.

This was especially noted towards the close of hostilities, so that by that time amœbic dysentery could be regarded as endemic amongst the British, with a high proportion of relapses.

Such statistics as are available from East Africa show a proportion similar to the records from Egypt, though the incidence of amœbic dysentery, according to Hughes, was higher amongst the native porters.

Manson-Bahr's observations in Egypt and Palestine, as well as those of Gunn and Savage, indicate that the amœbic dysentery rate amongst troops in the field appears to be at its highest during the first three months of the year, that is, at a period when the bacillary disease is in abeyance, and, on the whole, the experiences of Mesopotamia would seem to bear this out.

A vast amount of illuminating work, mainly by Wenyon and Dobell, has been done during the war upon the morphology and life history of the intestinal amœbæ.

The discovery of amœbæ in dysentery stools was made by Lösch in 1873, and since then they have been the subject of much study. It is now recognized that several distinct amœbæ are present in the intestinal canal of man, of which only *Entamœba histolytica* is pathogenic. The others are harmless species. Owing to the number of species of intestinal amœbæ and the necessity of being able to recognize the one pathogenic species with certainty, it is most necessary that, in making a diagnosis of amœbic dysentery, the pathologist should have some insight into modern intestinal protozoology. The main practical points to remember are that the *Entamœba histolytica*, if the cause of the dysentery, is generally very active and contains as a rule, ingested red corpuscles. The nucleus can rarely be distinguished in the unstained state; most usually the organisms show a differentiation into a granular endoplasm and a clear hyaline ectoplasmic zone.

The causes which predispose towards the development of amœbic dysentery are not yet accurately understood. They are probably in the main similar to those which produce the more acute bacillary disease. The experience of the war, supported by experimental data upon the survival of *E. histolytica* outside the body, supports the idea that the principal medium for the production of amœbic dysentery is a polluted water supply. A continuous high and moist temperature appears to be favourable to the development of the disease and would explain, in part at any rate, the undoubtedly greater prevalence of amœbic dysentery in tropical and subtropical countries.

Morbid Anatomy.

With regard to the morbid anatomy of amœbic dysentery, the action of the entamœba on the tissues is, to a great extent, mechanical, although there is, in addition, a localized lytic action, and death may take place in many ways, commonly through perforation of the gut wall, though it may be due to exhaustion or hæmorrhage. The earliest lesions consist of minute yellow hemispherical elevations of the mucosa, which by breaking down become converted into the typical flask-shaped amœbic ulcer of which the tissues of the submucosa form the base. The ulcers are confined to the large intestine and generally commence in the cæcum, but they may occur anywhere throughout the large intestine, especially in the transverse and pelvic colons. As the lesions progress in size they may coalesce to form large patches of several inches in extent. There is usually a considerable degree of compensatory hypertrophy of the bowel wall.

In early cases the intervening mucous membrane remains to all appearance normal and healthy. In chronic cases the whole mucous membrane may be involved, with the formation of polypoid or even gangrenous masses, which project into the lumen of the bowel.

The individual ulcers are generally covered with yellow, greenish or even black sloughs, which may adhere to the underlying granulation tissue. Thrombosis of the blood vessels occurs at the bases of the ulcers, and as ulceration extends deeply a fair-sized blood vessel may be eroded and a severe or fatal hæmorrhage may result. Perforation or even massive gangrene of the gut may terminate in purulent peritonitis. The site of perforation is usually the cæcum or transverse colon.

The entrance of the amœbæ into the tissues is thought to take place through the crypts of Lieberkühn into the submucous tissue, when, by means of cytolysins, which they secrete, they produce a gelatinous and œdematous tissue necrosis. As compared with the bacillary lesions the relative absence of inflammatory cell-infiltration is to be noted.

Symptoms.

The incubation period of amœbic dysentery is probably a long one. The only experimental evidence in this direction is the classical work of Walker and Sellards. There are many factors to be considered, but it is probable that from the time of entrance of the infecting material into the intestinal canal to the appearance of recognizable symptoms of dysentery a long period elapses—an average of 64 days in the experiments cited—whereas the characteristic cysts appeared in the fæces nine days after infection. It may therefore be justifiably stated that the more chronic protozoal, as compared with the more acute bacillary infection, has a correspondingly longer incubation period.

The symptoms of amœbic dysentery are protean, for it has long been known, and has been emphasized by the post-mortem findings of Bartlett during the war, that a considerable ulceration of the intestine may be present without provoking any recognizable symptoms during life. Indeed, cases of this disease have been seen in which sudden perforation took place with few, if any, premonitory signs. For example, in the case of a medical officer in excellent physical condition, whose symptoms consisted solely of an occasional attack of diarrhœa, perforation of the cæcum took place suddenly with a fatal result.

The great majority of cases run a chronic course with frequent relapses, alternating with periods of chronic constipation. Acute and even choleraic clinical forms of amœbic dysentery do, however, occur, and in these cases the symptoms may be indistinguishable from bacillary dysentery. But as a general rule, the abdominal pain and tenesmus are much less acute and tend to be localized to certain spots, such as the cæcum or transverse colon. The pain may closely simulate that of appendicitis, and may therefore suggest surgical interference, but the surgeon should always be on his guard against this.

The stools are as a general rule larger than those of bacillary dysentery, but are usually not so numerous. They may contain a considerable quantity of dark and altered blood, which imparts to the motions a penetrating fœtid odour, and when the gut has become gangrenous actual sloughs may be found.

Unless the case is complicated by hepatitis, there is seldom any fever, and no symptoms of toxic absorption are present. The latency which this disease exhibits is one of its most striking characteristics. Often without treatment all symptoms may subside and the patient may regain condition, only to relapse again, it may be, after an interval of months or even years.

The experience of the later period of the war has strengthened the idea that amœbic infection is specially prone to supervene upon a previous bacillary attack. It is well to bear in mind that chronic diarrhœa in a patient convalescent from the latter disease, whether mucus is present in the stools or not, may possibly be an amœbic infection.

Death in amœbic dysentery may result from exhaustion, uncontrollable hæmorrhage, perforation of the intestine or liver abscess. The hæmorrhage may be sudden, profuse, and is often fatal ; it may even occur in men who have not previously shown evidences of infection.

Prognosis.

The question of prognosis in amœbic dysentery is a subject which is very difficult to treat adequately. It is impossible to prognosticate with any degree of certainty what the course of an amœbic dysentery is to be. Possibly the great majority of cases, if recognized early, are amenable to treatment, and these cases may be considered fit for further active service. On the other hand, a case which has relapsed more than once is unfit for active service, especially since recrudescences of the disease are produced by physical exhaustion and dietetic indiscretions. As a pensionable disease, undoubtedly amœbic dysentery has a greater claim to recognition than has the bacillary form. Convalescents from the latter usually entirely recover their digestive and absorptive faculties. Amœbic convalescents, on the other hand, especially if the fæces still contain the characteristic cysts, must be regarded as still infected and therefore liable to relapse. The possible dangers of sudden perforation or complication of liver abscess should also not be forgotten. Moreover, often actual mechanical alterations of the bowel wall, in the shape of adhesions, cicatricial bands, dilation of the colon and partial stenosis, may ensue as the result of extensive healed amœbic ulceration and may give rise to dyspepsia and chronic intestinal stasis. All these conditions and possibilities should be taken into account in assessing the pension of a man convalescent from amœbic dysentery.

The clinical distinctions between the two main forms of dysentery cannot always be relied upon and the final decision must rest with the pathologist. Considerable assistance may be obtained from the macroscopic appearance of the stools, though it is a dangerous proceeding in military practice to consider this as final. The laboratory diagnosis depends upon the ability of the observer to differentiate *Entamœba histolytica* from the non-pathogenic amœbæ and from macrophage endothelial cells. The entamœbæ are not uniformly distributed throughout the stool ; they are most readily found in the mucus and are not usually present in the fæces. They may even be excreted intermittently. It is often possible to find them in large numbers in one specimen and to be unable to do so in subsequent examinations. Therefore any opinion based upon a single fæcal examination is open to many fallacies. Should suspicion as to the nature of the case be aroused, it is as well to consider no result as negative until the stool has been searched on each of seven consecutive days.

Considerable assistance may be derived from a study of the cellular exudate of the stools, a point upon which emphasis has been laid by Willmore and Shearman. As a general rule the amœbic exudate consists of large numbers of red cells in rouleaux, few pus cells or endothelial cells being present. On the other hand much evidence of tissue destruction, in the shape of fragmented cells and extruded nuclei may be seen. Search should be conducted with a $\frac{1}{6}$ in. lens and the *Entamœba histolytica* identified by its activity, its characteristic appearance, and its ability to ingest red blood corpuscles. When hæmorrhage has been profuse, it may be impossible to detect any of the organisms. In the more chronic and latent stages the characteristic cysts may be present in large numbers and the detection in the stools is rendered easier by staining with Weigert's iodine, which shows up the nuclear structure, the contained chromatoid bodies and the glycogen vacuoles. When doubt remains as to the diagnosis the cysts may be stained by a rapid method introduced by Dobell; this is especially important in carrier cases.* The more extensive employment of the sigmoidoscope, by the routine use of which the characteristic amœbic ulceration in the lower part of the bowel may be recognized, even in cases where laboratory diagnosis has failed, is strongly recommended by Manson-Bahr.

Treatment.

The war led to several improved methods in treating amœbic dysentery. No hard and fast rule can be laid down for the treatment of every case, but as in the case of bacillary dysentery special symptoms must be met as they arise. The specific drug in this case is ipecacuanha or its derivatives. Although there are four alkaloids of ipecacuanha—emetine, cephæline, pyschotrine, and emetamine—the first alone appears to exert any specific action upon *E. histolytica;* but the manner in which it does so is not by any means understood, while it has no effect upon the non-pathogenic amœbæ living in the intestine. The experimental work of Dale and Dobell upon this point has not confirmed the original observations of Vedder and Rogers upon the toxicity of emetine to entamœba *in vitro*, but it is possible that direct observations of this nature do not constitute a sure guide to its action in the human body. All evidence shows that the judicious treatment of the patient with emetine in some form or other is the only measure likely to secure radical cure, but if it is given in insufficient dosage, or by unsuitable methods, the effects are temporary only. The drug should not, however, be given without due consideration being paid to its possible toxic effects. Experimental evidence, as well as clinical observation, has shown that excessive doses may give rise to an intractable diarrhœa and considerable asthenia, with a curious desquamation of the skin.

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* This method consists of fixation for ten minutes in Schaudinn's fluid, passing through two washes of 70 per cent. alcohol and iodine, ten minutes each, staining in Mayer's hæmalum for fifteen minutes, blueing in water, passing up through alcohols and xylol and mounting in the usual way.

Emetine treatment should be controlled by means of frequent and repeated stool examinations. The drug is best given hypodermically, or intra-muscularly, in individual doses of 1 grain each (1 gr. in 1 c.c. distilled water), and repeated daily for 12 days. The efficiency of emetine is considerably supplemented, according to Wenyon and O'Connor, if combined with oral administration of the same drug in ½-grain doses by the mouth. Vomiting may be readily induced by this means but this does not necessarily hinder the action of the drug on the entamœba. If the patient remains constipated, as he seldom does under emetine treatment, it may be advisable to combine it with small doses of sodium sulphate.

The double iodide of emetine and bismuth (emetine bismuth iodide), which contains 26 per cent. of the emetine alkaloid, was introduced by Dale in 1916 and is especially useful in chronic intractable cases and in cyst carriers. The drug is given in three-grain doses in gelatine cachets every night for twelve consecutive nights, but, when taking it, the patient should remain in bed and have a liquid, preferably milk, diet. Treatment should be controlled by daily and repeated microscopic examinations of the fæces for cysts. In intractable cases it may be necessary to administer two or more courses of the drug with a week's interval between each.

Specially difficult to deal with are those cases which resist every form of treatment by emetine. There are exceptional cases, which have continued to pass blood or mucus stools containing active entamœbæ after five or even more courses of emetine bismuth iodide. One case has been observed which continued to do so after sixteen courses. In such cases, it is possible that intravenous injections of neoarsenobillon in 0·4 grm. doses, combined with emetine bismuth iodide, as carried out by Brug, may help.

Vomiting and nausea when taking emetine bismuth iodide may be prevented by small doses of tinct. opii 10–15 min. given half-an-hour beforehand. The action of emetine bismuth iodide is not yet understood. Dale and Dobell have shown that it fails to cure amœbic dysentery in experimentally infected cats, while it was inconclusive in puppies infected in the same manner.

Some observers have recorded cures with chaparro amargosa, an infusion of the Mexican drug, *Castela nicholsoni*, in cases resistent to emetine. It is best given in the form of tea ; three teaspoonfuls of the powdered chaparro are boiled and strained. The oral administration may be supplemented by enemata of the same decoction given twice daily.

During the course of an attack of amœbic dysentery or subsequent to it, hepatitis, or actual hepatic abscess may supervene ; these constitute the most frequent complications of amœbiasis. Inflammation of the liver with considerable congestion and enlargement of the organ may occur in the height of the attack and is generally accompanied by evening pyrexia, and, it may be, rigors and sweats. Active treatment consists of repeated doses of emetine, saline aperients, fomentations, cupping and counter-irritants. There is considerable evidence that aspiration of the liver and abstraction of blood have a very beneficial effect in this condition.

The relationship between amœbic dysentery and liver abscess is now unquestionable. The two conditions often co-exist in the same patient, and it has been abundantly proved that they are caused by the same parasite. In most cases of hepatic abscess a previous history of dysentery or prolonged diarrhœa may be obtained. As a general rule a period of several months elapses from the time of the dysenteric attack until the formation of the abscess, and, according to Low, an interval of even 20 years may intervene. It has generally, however, been considered a somewhat rare complication, and war experience has so far borne this out. Cases of amœbic abscess have been reported from Gallipoli, Egypt and especially from Mesopotamia, but probably a number of cases will occur two or more years after the original infection, and may therefore only reappear amongst men who have been demobilized and returned to civil life.

The most important signs and symptoms of hepatic abscess are a history of a septic pyrexia, continuous or remittent with cachexia, anæmia and sweats, with a uniform enlargement of the liver, most usually in an upward direction, and it may be with local tenderness, rigidity over the right rectus, and signs of irritation or pressure at the base of the right lung. Very often a referred dull aching pain in the right shoulder, more noticeable at night time, is present. The leucocytosis, it should be noted, is generally moderate, on an average 18,000, but an increase of leucocytes is not necessarily present. Candler, for instance, has operated on one in which there was actually a leucopenia. X-rays, by demonstrating a limitation of movement of the right dome of the diaphragm, may assist in diagnosis.

The amount of ulceration of the bowel associated with hepatic abscess may be minimal, and too much stress must not be laid upon the presence of *histolytica* cysts in the fæces of these cases, as they are often absent. When present they are to be regarded as supplying only confirmatory evidence of a suspicion based upon the clinical signs and symptoms.

Absolute diagnosis should be made by aspiration in search for pus through an area of dullness, preferably between the 7th and 8th ribs in the mid-axillary line. The needle should be thrust in an upward as well as inwards direction and sustained traction on the piston maintained as it is withdrawn.

All evidence so far accumulated tends to show that, when once pus has formed, the condition can no longer be cured by emetine, though, from the success of the drug in amœbic hepatitis, the formation of pus may possibly be prevented.

The recent work of surgeons on this subject would seem to indicate that, whenever the abscess is of moderate size and can be localized, the aspiration of the liver pus by means of a large aspirating syringe or evacuation by Potain's aspirator and subsequent injection of 3–5 grains of emetine in saline into the abscess cavity, with the idea of destroying the contained entamœbæ, is preferable to the open operation. It is true that re-accumulation of the pus sometimes occurs, but the ease with which it can be located and evacuated once more renders the repetition of the operation a very simple matter. Recovery is very rapid; there is no open wound and the risk of septic complication is reduced to a minimum.

According to Armitage 48 cases of amœbic abscess of the brain have been recorded, for the most part from Egypt. The abscess is generally solitary and may be regarded as a metastasis of hepatic abscess. During life it gives rise to various cerebral pressure symptoms, and is invariably fatal. One such case, in a New Zealander, has been recorded during the war by Stout, Fenwick and Armitage.

Prevention.

As in the bacillary disease preventive measures directed against the spread of the *Entamœba histolytica* from one person to another depend upon general sanitary conditions, but there is a special point in which the control of the amœbic disease presents difficulties, and that is the carrier question.

Carriers of *E. histolytica* may be divided into two classes, the contact carrier who has never suffered from amœbic dysentery, and the convalescent carrier who has recovered from such an attack and who continues to pass numbers of *E. histolytica* cysts in his fæces.

The comparatively large number of contact carriers amongst the population of temperate as well as tropical countries, has been greatly emphasized during the period of hostilities, and a large amount of work has been devoted to this subject by British protozoologists. It is now easy to understand how it is that *E. histolytica* is the cause of amœbic dysentery and hepatic abscess and yet does not produce disease in the majority of individuals harbouring it; and how these diseases are not contracted from the person in the acute stages of his illness but from the apparently healthy carrier. For every abnormal individual suffering from amœbic dysentery there are many comparatively healthy carriers passing cyst-containing fæces infective to others.

There can be little doubt, however, that, whether *E. histolytica* causes dysenteric symptoms or not, it must live at the expense of the tissues of its host, and one must suppose that even the healthy carrier has the mucosa ulcerated, although the damage may be so minute as to be almost invisible.

Amongst British soldiers after a year's active service in Egypt, which is notoriously a home of amœbic infection, Wenyon and O'Connor found no marked difference between the incidence of carriers among those who had previously suffered from dysentery and those who had not, the percentages being 6·5, as against 4·5 per cent., though amongst native Egyptians it was considerably higher.

The carrier rate will necessarily vary considerably, as Dobell has pointed out, according to the number of times each individual is examined, as it is known that *E. histolytica* cysts are but intermittently excreted; it is probably necessary to examine the fæces on at least six separate occasions before pronouncing an individual free from infection, though it is estimated that two-thirds will be found at the first examination.

Examining a series of convalescents in this manner, Dobell, Gettings and Jepps showed that the percentage of carrier cases was highest in the Mediterranean and Mesopotamian war zones.

The figures are as follows:—

France	8·37 per cent.
Salonika	18·92 ,, ,,
Egypt	18·96 ,, ,,
Gallipoli	23·07 ,, ,,
Mesopotamia	20·51 ,, ,,

One of the most surprising outcomes of the systematic fæces examination by protozoological experts during the war has been to show the widespread presence of *histolytica* carriers in England. Malins Smith has shown that 4·2 per cent. of the lunatics at Rainhill Asylum were carriers, and after an extensive enquiry amongst recruits under training he also found that 5·6 per cent. were carriers, and amongst naval ratings the rate was estimated at a slightly lower figure.

From a consideration of the above-stated facts, it would be a counsel of perfection to examine large bodies of men under active service conditions, so as to identify the carriers of infection and to seek to eliminate them by effective treatment with emetine bismuth iodide. Obviously, this is quite impracticable and, besides, one cannot by any means control the highly parasitized natives of countries such as Egypt and Mesopotamia with whom the soldier may be brought into daily contact. The majority of the carriers are perfectly healthy; the percentage of those who actually develop a condition of amœbic dysentery is not accurately known. When every able-bodied man is needed for war service, it is unreasonable therefore to detain any individual, whether convalescent from dysentery or not, just because he happens to be a carrier of *E. histolytica*. It is possible, however, to ensure that no gross carrier is employed as a mess cook or in any way connected with water duties.

The actual method of transference of *E. histolytica* from one man to another is as yet a matter of conjecture. Probably a considerable amount of infection takes place through mechanical transference by house-flies, as has been shown by Wenyon, O'Connor and Buxton. The two first-named investigators proved that these cysts do not degenerate in the fly's intestine and may be found there as long as any fæcal matter remains. The direct passage of the fæcal material through the alimentary canal of the insect takes but five minutes, and would seem to be of more importance in the dissemination of the disease than regurgitation of material through the proboscis.

One thing is certain, that moisture is absolutely necessary to the vitality of the cyst; if dried it immediately dies. There is little doubt, on epidemiological grounds, though unsupported by any direct evidence, that amœbic dysentery is spread by water infection, and it is probably due to the careful sterilization of the water supply in Egypt and Palestine that the amœbic dysentery rate was comparatively low.

As in the bacillary disease the essential precautions consist of measures directed against the house-fly as well as careful supervision of the water supply.

BALANTIDIAL AND OTHER FORMS OF DYSENTERY.

The differential diagnosis of the dysenteries entails a knowledge of all those conditions in which blood and mucus may appear in the stools. The following is a short résumé of the conditions which may possibly be mistaken for the better-known forms of the disease.

A blood-stained mucopurulent discharge may be passed in infestations with *Schistosoma mansoni*, *S. hæmatobium* and *S. japonicum.* Instances of the two former came under notice in troops infested with schistosomiasis in Egypt. Dysenteric symptoms are apt to supervene two to three months after infestation. The typical stools contain yellow or bile-stained mucus with clots or streaks of blood in which schistosome ova, generally lateral-spined, may be found under low power of the microscope. The presence of a high eosinophilia in the blood in a case with symptoms of subacute dysentery and, it may be, a previous history of pyrexia and urticaria, should make one suspect schistosomiasis. Amongst Egyptian troops and labour corps schistosomiasis accounted for 5 per cent. of all clinical dysenteries. But, of course, schistosomiasis may co-exist with either the bacillary or amœbic dysentery. Blood and mucus may also be passed in infestations of the intestinal canal with *Ascaris lumbricoides* or *Ankylostoma duodenale,* and also in Nigeria with a rare sclerostome of man known as *Œsophagostomum apiostomum.*

Dysentery due to infection with a large infusorian known as *Balantidium coli* is a rare disease. The pathology and clinical symptoms resemble those of amœbic dysentery. It has been reported from the Philippines, Germany, France and Russia, mainly in those intimately associated with pigs, as this animal appears to be the reservoir of infection. This parasite has rarely been observed in cases from Gallipoli at Mudros, and once in Egypt, during the war ; but in neither of these instances was it associated with the clinical symptoms of dysentery. There is one record by Payan and Richet of an acute and fatal case occurring in a Serbian soldier in France.

There is considerable doubt whether the protozoon *Giardia* (*Lamblia*) *intestinalis* is to be regarded as pathogenic. It is an inhabitant of the small intestine and may appear both as active forms and cysts in enormous numbers in the fæces. It is generally associated with diarrhœa, though occasionally bile-stained mucus may be present. It is believed by many investigators that when present in large numbers it can give rise to an explosive diarrhœa associated with abdominal discomfort, but except as a matter of medical interest it is of little importance from the military point of view.

With regard to malarial dysentery, a word of caution is necessary. Graham and Logan state that many cases of dysenteric symptoms in association with malaria, especially of the subtertian type, are really due to a concomitant infection with the dysentery bacillus, but one should also note that intestinal hæmorrhage associated with rigors, icterus and abdominal pain may occur in the course of a severe subtertian infection. In these cases the subtertian rings have been found in stained smears prepared from the stool. Much altered and even bright red blood may appear in the fæces and thus influence the medical officer on clinical grounds to disregard the malarial element. The prognosis in these cases is grave, and, directly a diagnosis is established by microscopical examination of the blood, quinine therapy should be instituted.

Certain other conditions may give rise to blood and mucus in the stools. Such are non-specific colitis, both of the membranous and ulcerative varieties, tubercular ulceration of the bowel, syphilitic disease, and even simple polypus of the rectum. It is surprising how often in military practice blood from internal or external piles, passed with the fæces, is mistaken for true dysentery. In such cases the blood is freshly passed, the fæces are generally formed and scybalous, and therefore no great difficulty should be experienced in making a correct diagnosis.

Finally, it is possible that acute types of bacillary dysentery may be mistaken for Asiatic cholera, food poisoning, or infections with *Bacillus gaertner* or *aertrycke*, in which conditions blood may be passed in the fæces, especially during the early stages of the illness.

Under active service conditions, when the means of obtaining a laboratory diagnosis of such a complex subject as dysentery are difficult to procure, the following points may be taken as a guide in the routine management of cases of clinical dysentery, in order to ensure adequate treatment at the earliest possible moment.

(1) A clinical dysentery, especially if acute and occurring suddenly, is probably of the bacillary type. The patient is therefore a source of danger to his fellows and should be isolated as soon as possible. Such a case should be given a full dose of anti-dysenteric serum without waiting for the pathological report. Whatever the type of case may be, the serum can do no harm, and, in the bacillary disease, there is ample evidence to show that any delay is unwarrantable, for it may entail irremediable damage to the intestinal canal.

(2) Blood and mucus in the stools mean dysentery. The exudate should be reported upon by a competent pathologist at the earliest possible moment.

(3) A diagnosis of dysentery and the actual presence of blood and mucus must be legibly recorded, or, still better, stamped, upon the man's field medical card before evacuation and the appropriate treatment at once instituted. This, unless strong indications to the contrary are forthcoming, should be subsequently adhered to. In other words, a dysentery once diagnosed amœbic should be assured continuous emetine treatment, or, if bacillary, a continuance of saline aperients.

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CHAPTER IV.

CHOLERA.

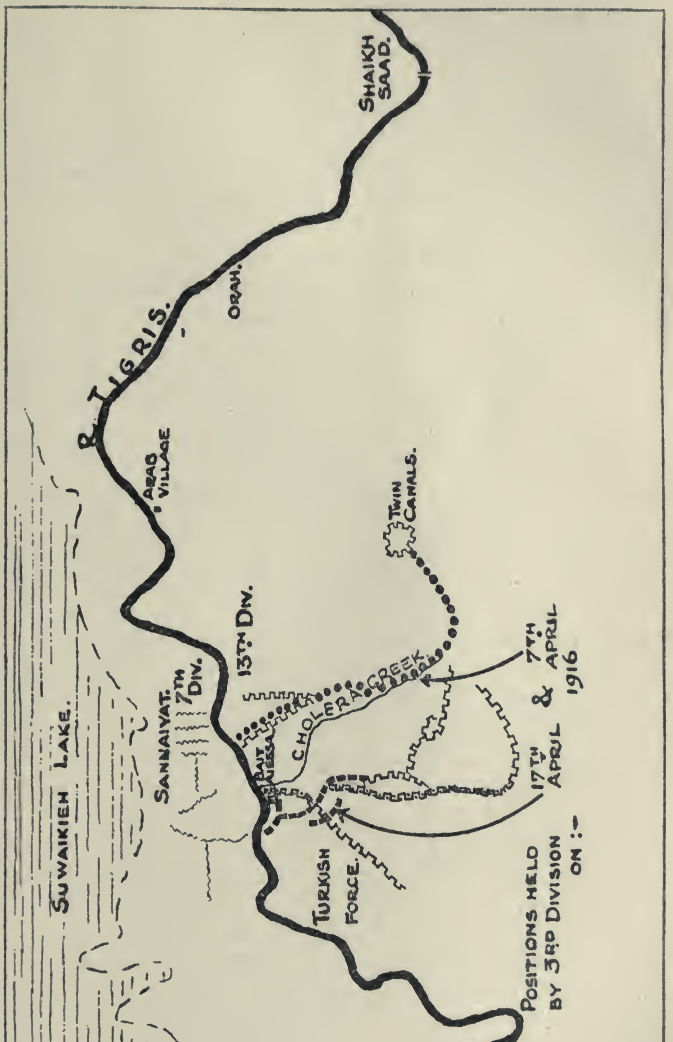
IN July 1914 cholera occurred in the Russian provinces bordering on Galicia. The first cases in the Austro-Hungarian army operating in Eastern Galicia appeared on 20th September, 1914, and by the end of 1914, 22,000 cases with 7,672 deaths had been reported ; by September 1915 the numbers had increased to 26,000 cases with 15,000 deaths. It is known that Austria employed certain divisions from Galicia to invade Serbia in 1914, and in all probability these troops were responsible for conveying the infection into Serbia, as a great epidemic broke out there in 1914. By September of that year 12,000 cases had been reported in the Serbian army, with a daily proportion of fresh cases varying from two to three hundred.

The German army co-operating with the Austro-Hungarian troops in Galicia is stated to have suffered severely from cholera, while the German troops operating against Russian Poland were also affected by the disease. The chief outbreaks in the German army were in December 1914 and August 1915, and it is recorded that 13 cases occurred among the German forces on the Western Front, 78 cases among German civilians, and 3,166 cases among Russian prisoners of war between November 1914 and November 1915. Although total figures for the German army are not given, ratios of 0·65 per 1,000 of strength in the field army, and 0·05 in the reserve army, have been published.

In Turkey there was no record of any outbreak of cholera during the year 1915, but in the spring of 1916 many epidemics were reported from different areas. It has been stated that between May 1916 and 14th February, 1917, there were in Jerusalem and the surrounding villages 183 cases and 116 deaths, in Baghdad 179 cases and 76 deaths, in Mosul 130 cases and 51 deaths, and in Aleppo 2,020 cases and 1,203 deaths.

In Persia three cases occurred at Kazvin during November 1915, and 10 cases and seven deaths at Kermanshah during July 1916.

Although the British troops were operating in areas where cholera was endemic, and in contact with infected allies and enemies, they were affected by cholera only in Mesopotamia and Sinai, where 2,852 and 28 cases occurred respectively. Knowledge of the spread of the disease in the British armies during the war is derived from what took place in thes countries



DIAGRAMMATIC MAP SHOWING CHOLERA CREEK AND POSITIONS OF BRITISH TROOPS.

Fig. 1.

On 17th April, 1916, the British force operating on the Tigris for the relief of Kut, attacked and occupied the Turkish position at Bait Aiessa, and it was known that cholera had broken out in the Turkish force operating in front of Kut. A glance at the map in Fig. 1 shows the position of the water creek which ran south-east from Bait Aiessa through the Turkish lines to the British trenches, and which afterwards became known as Cholera Creek on account of the infection it had bred.

The water in this creek was polluted by fæcal matter and corpses, and consequently when the British troops, suffering from fatigue, heat and thirst, drank its unsterilized water, they became infected. Cholera broke out in the 3rd Lahore Division on 25th April, and spread to the 7th Meerut and 13th British Divisions. Up to the middle of June, when the epidemic had practically subsided, the total number of cases admitted to hospital from the 3rd Lahore Division was 66, from the 7th Meerut Division 62, and from the 13th Division 249.

Nomadic Arabs kept in close touch with the flanks of both forces, and, contracting the disease, they probably disseminated infection in other districts through their wanderings.

At first no special field ambulance or casualty clearing station was detailed for cholera cases, nor were any preventive measures or schemes drawn up by headquarters, although in other theatres of war this had been done. All the field ambulances were crowded with sick and wounded, and officers commanding units experienced a shortage of both tents and personnel, so that the measures which could be adopted for segregating and isolating doubtful cases of cholera and contacts were limited. A certain number of doubtful cases were evacuated down stream by river boats, and there is no doubt that infection was carried in that way.

The last considerable group of cases reported in the forward area occurred on the river steamer " P50.," when 33 cases from the 105th Maharatta Infantry were sent to hospital at Sheikh-Saad in mid-August. In September seven cases, and up to 10th October four cases, were treated in the cholera hospital at Sheikh-Saad. The majority of these cases contracted the disease on river steamers coming down from the front area. The outbreak on " P50 " was traced to the water supply. The drinking water was sterilized by means of steam from the engine and the tanks were filled from the river by a steam pump. The arrangements were not carried out satisfactorily, and the Indian personnel of " C " and " D " Companies frequently drew water direct from the river below the latrines, which were situated about mid-ship. (See Fig. 2.)

In consequence of this outbreak, the question of the position of the cooking places was considered and investigated by the Deputy Director Inland Water Transport, and it was arranged that they should be placed forward instead of aft.

There were 501 cases at Amara between 29th April and 1st December, 1916, and between 24th and 31st August, 1916, there was an acute epidemic in two of the hospitals stationed there. Thirty-five cases, with 14 deaths, were reported from No. 1 British General Hospital, and 19 cases, with 10 deaths, from No. 23 British Stationary Hospital. In both hospitals infection was carried by the milk supply. The milk was sterilized before it was given to hospital patients, but unfortunately it often arrived late, and the sterilization was not always supervised.

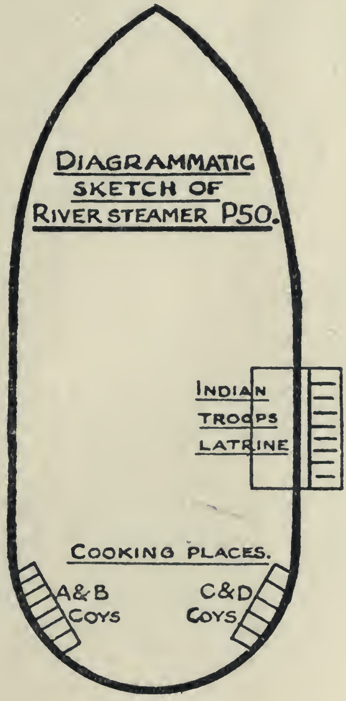


Fig. 2.

In Basrah, from April to November 1916, 673 cases of cholera were admitted to the hospitals and 246 cases died. The first cases were notified on 1st May, 1916, and the water supply was found to be the cause of the disease. At No. 9 and No. 10 Indian General Hospitals there was a sharp epidemic in October. It was suggested that the milk had been infected, but it was discovered that only the men who were not confined to bed were attacked, and that those who were confined to bed and lived on a milk diet escaped. The infected men had drunk polluted water from a neighbouring creek in which bedpans had been washed by the hospital sweepers.

Cases were reported in June 1916 from the 15th Indian Division stationed at Nasiriyeh on the Euphrates. Twenty-eight cases were admitted to hospital between June and September and there were 19 deaths. There were 180 cases amongst the civilian population. Investigation showed that the outbreak was due to infection which was water-borne, and that Arabs from the Tigris front had carried the germs of the disease to the villages situate upstream of Nasiriyeh.

In the summer and autumn of 1917 a considerable number of cases of cholera was reported from Baghdad, Basrah and Nasiriyeh. When the British force captured Baghdad in March 1917, the Turkish water pumps were taken over. These pumps delivered crude river water from seven different intakes into nine different pipe lines, which gave a limited and intermittent supply to every part of the city. It is interesting to record in connection with the Baghdad cases that, although automatic chlorinators were fixed to all the intakes of the water supply for Basrah early in 1917, it was not until April 1917 that one was taken to Baghdad, and they were not made use of there till November 1917, when the epidemic of cholera, which claimed General Maude as one of its victims, was shown to have sprung from the river.

In 1918 cholera epidemics were reported among the Arabs, and the infection spread to the 13th, 14th and 15th Divisions, appearing also in Basrah and Baghdad. The number of cases reported between May and December 1918 was 69 in the 13th Division, 28 in the 14th Division, 5 in the 15th Division, 141 in Basrah, 147 in Baghdad, and 1 in the Sheikh-Saad-Kut area.

The occurrence of cases of cholera among the Turkish forces in Syria first became known to the Egyptian Expeditionary Force in July 1916, after the commencement of the British advance from the Suez Canal into Sinai. On August 4th, 1916, the Turkish attack, threatened since the middle of the preceding month, developed at Romani and Katia and continued during the next two days. The enemy were heavily defeated, and retreated, pursued by British troops.

During the month of August the heat in the Sinai desert was very great, but every effort was made to provide a gallon of sterilized water per man per day, each mounted man being given two water bottles, although it was sometimes impossible during the fighting and pursuit to get the water camels out to the troops.

Maintenance of water discipline was difficult in men exhausted by long working in the sand and heat of the desert, and after the capture of the oasis of Katia men of the 157th Brigade drank water from shallow wells which had been used by the Turks, without waiting to sterilize the water by means of soda bisulphate tabloids with which each man was provided. The enemy had just been driven from this oasis, leaving the surroundings of the wells and the whole area in a very foul condition. Certain men of the Anzac Mounted Division, during the pursuit of the Turks, also drank water from Turkish water barrels found in deserted oases. The first case of cholera occurred in a non-commissioned officer of the Anzac Mounted Division on 7th August, and subsequently 25 further cases were admitted to hospital at various dates up to and including 23rd August, after which date no more cases occurred.

Ætiology.

All recent evidence shows that the cause of cholera is infection with the cholera bacillus, which is taken into the body by the mouth by means of infected food or drink. The small outbreak which occurred in the Egyptian Expeditionary Force after the battle of Romani (Katia) in 1916 and the outbreaks in Mesopotamia were due to drinking infected water.

The cholera bacillus has but feeble resisting powers outside the human body and soon dies if dried. If, on the other hand, it is kept moist it will live for a considerable time, as, for instance, on the surface of fruit or vegetables if not exposed to the sun; and, as shown by Major Greig, I.M.S., it can exist in moist fæces for as long as seventeen days. The cholera bacillus soon dies in sterile water, but has been recovered from natural water within a period of 56 days. The cholera bacillus cannot as a rule be found in the fæces of patients for more than a few days— 10 days at the most— after recovery from an attack, but occasionally patients have harboured the bacillus for a month or more.

In recent years a considerable amount of research has been carried out as to the possibility of the disease being conveyed by means of cholera carriers. It has been found that during cholera epidemics the stools of healthy persons may contain true cholera bacilli, and that therefore the cholera carrier is an important factor in the spread of the disease. Examination of contacts is therefore essential during any epidemic of cholera, and the discovery and control of carriers is all-important. These facts were well recognized during the war, and both in Mesopotamia and Sinai the examination of cholera contacts was carried out as a preventive measure.

The cholera bacillus may be isolated *post mortem* from the tissues such as the lungs and biliary passages, and may also be found in the liver, spleen, kidneys, and heart muscle and in large numbers in the mesenteric glands. The vibrio may be detected in the whole of the biliary tract from the gall bladder to the common bile duct. This last fact is of interest in connection with the question of carriers.

Symptoms.

The incubation period lasts from a few hours to two to six days. It is usually 24 to 48 hours. Observations, however, of cases during the war seemed to show that the incubation period might be prolonged in those who had been inoculated against the disease.

It is usual to describe the clinical course and symptoms of a case of cholera under three headings, namely, the stage of evacuation, the stage of collapse, and the stage of reaction; but it must be borne in mind that the three stages are not sharply divided but pass insensibly one into the other.

The signs and symptoms of a typical acute attack of cholera in any of its three stages are well known and need not be fully described. Certain variations from the ordinary may, however, be met with during an epidemic.

Cholera sicca is an acute and almost invariably fatal form of the disease, but it is fortunately of infrequent occurrence. In it collapse takes place with little or no evacuation from the bowel, though the intestines may actually be distended with fluid. Sudden death may occur from cholera sicca, and such cases may present very great difficulties in diagnosis.

In certain severe cases of ordinary cholera, even in those ultimately proving fatal, though diarrhœa is present and prostration marked, the stools may fail to show the typical rice-water appearance, and may resemble those met with in an ordinary attack of gastro-enteritis, and may even contain blood.

The following complications and sequelæ may occur during or after the stage of reaction in an attack of cholera: excessive febrile reaction, uræmia, pneumonia, dysenteric diarrhœa and rash.

Prognosis.

The mortality in different epidemics has varied considerably. An average mortality in former epidemics may be considered to have been 50 per cent., but with the modern treatment introduced by Sir L. Rogers the average mortality has been reduced below that figure. Young persons and old people have a high mortality, as have those also who suffer from kidney disease. Chronic alcoholism is very unfavourable. The mortality in the Sinai outbreak in 1916 was 25 per cent. ; in Mesopotamia during 1916 the mortality amongst all British and Indian cases occurring in the 3rd, 7th, 13th and 15th Divisions was 41·4 per cent., and amongst cases in Amara it was 36·9 per cent. In 524 Indian cases at Basrah in 1916 it was 33·7 per cent. In the 13th Division (British) of 249 admissions, 102 died, or 40·9 per cent. Finally, in 344 British and Indian cases admitted from 1st June, 1918, to December 1918, the mortality was 40·55 per cent.

In the cases which recover permanent ill-effects are at the most very uncommon, and no disability giving any claim to pension or compensation should arise.

Diagnosis.

Diagnosis during an epidemic of cholera is usually simple and should not present difficulty, but sporadic and atypical cases are less easy of recognition. In the East any sudden attack of severe diarrhœa and vomiting, particularly if attended with muscular cramps and prostration, should be regarded with suspicion, and the more so if it occurs during the cholera season, even though no previous cases have been reported. The signs on which the clinical diagnosis is usually based are the sudden onset, the character and copiousness of the stools and vomit, the prostration, the husky voice and the shrinking tissues. In mild cases the diagnosis may be impossible, or the disease not even suspected, without a bacteriological examination, as happened during the Sinai outbreak. Again, owing to active service conditions, cases may not be seen until the acute symptoms have passed and a state of febrile reaction exists. Such cases are liable to be mistaken at first for fever of the enteric group, and the diagnosis is very difficult, as the cholera vibrio may not be found in the stools. One case of this nature was seen in Sinai in which cholera bacilli were only recovered *post mortem* from the gall bladder, five previous examinations by three skilled observers having failed to show the presence of the vibrio in the stools. In all suspected cases, therefore, the fæces should be examined bacteriologically for the detection of the cholera bacillus. Serum agglutination tests are helpful in the detection of cholera carriers, as convalescents, especially when the disease has been mild, may show a high agglutination titre.

Certain diseases may be confounded with cholera, particularly when they have as symptoms or physical signs such affections as muscular cramps, cyanosis, shrinking of the tissues and so on.

Ptomaine poisoning, meat poisoning of bacillary origin, malignant malaria, acute bacillary dysentery and acute gastroenteritis (summer diarrhœa) in children, and poisoning with the irritant metals such as arsenic or antimony, may all produce symptoms having a resemblance to cholera. It is difficult to distinguish the premonitory diarrhœa of cholera from ordinary diarrhœa, and it is therefore of great importance during an epidemic of cholera to isolate all cases of diarrhœa if possible, or at any rate to make a bacteriological examination of the fæces.

Treatment.

In the treatment of premonitory diarrhœa all purgatives especially salines should be avoided. Rest in bed, warmth, and a suitable fluid diet are necessary. Astringents and bismuth salicylate are useful. Opium should not be given, as it may be harmful if the case should pass into the more serious form of cholera.

The treatment, which is now recognized as the most efficacious and which is founded on sound principles, is that first introduced by Sir L. Rogers. This treatment when properly carried out has reduced the mortality from 50, 60 or even 80 per cent. to 30 per cent. ; and in a recent large series of cases treated by Rogers the mortality was only 15 per cent. The principles on which Rogers' treatment is founded as laid down by himself are as follows. :—

(1) Whenever collapse occurs and the blood pressure falls to 70 mm. Hg., replace the fluids and salts lost from the body by hypertonic intravenous saline injections in sufficient quantity to raise the blood pressure to normal, adding alkalies to neutralize acidosis.

(2) Watch and control the temperature in the reaction stage.

(3) Continue to observe the blood pressure after the reaction, and maintain it at a level which ensures a free secretion of urine.

The indications for the composition and the technique of the intravenous and rectal injections are described in the pamphlet included in the official War Office cholera outfit. One or two points of importance may be mentioned.

During the stage of collapse in mild cases where the blood pressure is not below 70 mm. Hg. and the specific gravity of the blood is more or less normal (1,058 in Europeans, 1,055–6 in Indians), rectal injections of hypertonic solution combined with general treatment will suffice ; but a close watch must be kept on the blood pressure, and if it falls, recourse must be had to the intravenous injection applicable to the more severe cases. In the more severe cases the condition of the pulse affords the simplest indication for the necessity of intravenous injections, but it is much better to use the sphygmomanometer which is essential in the scientific treatment of cholera. If the blood pressure is found to be 70 mm. Hg. or lower, a hypertonic intravenous injection of three to six pints should be given. The specific gravity of the blood is another important guide to treatment, as if the specific gravity is 1060 or over and the blood pressure 70 mm. Hg. or less, a copious intravenous injection is required; and further, if the specific gravity is over 1065, even if the blood pressure is over 70 mm., an injection should be given.

Recent researches having shown the presence of acidosis in cholera, Rogers has modified the composition of his original hypertonic solution by the addition of sodium bicarbonate. It should be remembered that a bicarbonate solution is spoiled by boiling, and that the bicarbonate, sterilized by dry heat if necessary, should be added later to the sterilized water.

The indications for the use of the original or modified saline solution may be briefly stated as follows. If a patient is admitted within the first day of the disease, and there is no marked suppression of urine, the ordinary hypertonic saline injection (sodium chloride, 120 grains; calcium chloride, 4 grains; sterilized water, 1 pint), should be given in the first instance. But in all cases requiring a second injection, as well as in patients only coming under treatment late in the disease or with a deficiency of urine, one pint of water containing 60 grains sodium chloride + 160 grains sodium bicarbonate should first be injected, and then transfusion continued with the ordinary hypertonic solution. In mild cases, where only rectal injections are indicated, the combination of sodium chloride and sodium bicarbonate may also be used.

In addition to the treatment by injections the administration of permanganate salts by pill (two grains potassium permanganate) and in solution (calcium permanganate three to six grains to the pint) should always be carried out, as detailed in the official pamphlet. If the patient cannot take the permanganate drink or refuses to take it in sufficient quantity, barley water may be given in sips, as larger amounts of fluid taken at one time are apt to excite vomiting.

Rogers' treatment by means of hypertonic injections and the administration of permanganates is the standard treatment for cholera, but numerous other methods have been advocated from time to time, and one of the more recent for which success has been claimed is the so-called *bolus alba*. This consists of kaolin, that is, aluminium silicate powdered and free from gritty particles. It is given in water in a dose of 200 grammes (7 oz.) in 400 c.cs. (14 oz.) of water. If vomited, a second dose is given immediately in small sips. Atropine $\frac{1}{100}$ gr. may be given hypodermically night and morning as a routine measure in addition to other treatment, and Rogers recommends that atropine should be given immediately on admission.

If the treatment applied during the stages of evacuation and collapse is successful the diarrhœa and vomiting lessen or cease, the pulse returns, the body becomes warm, and the stage of reaction commences. The great danger during this stage is an excessive febrile reaction. It is well to take the rectal temperature after an intravenous injection, and, if this is found to be raised, a pint of iced normal saline should be injected by the rectum, and treatment by cold sponging generally and cold applications to the head undertaken. This treatment should be continued or repeated if required. Diarrhœa may sometimes occur during the stage of reaction, but unless excessive it should not be checked.

Post-choleraic uræmia is one of the most serious complications of the disease, but the liability to its occurrence will be lessened if the alkaline sodium bicarbonate injection has been given. The alkaline rectal injections should be continued after the collapse stage in all cases of suppression of urine until two pints of urine are passed in the 24 hours, and the patient should be encouraged to drink as much water, or barley water, as possible. Intravenous injections of the alkaline saline need only be resorted to if the flow of urine is not brought about by these measures. Additional means of treatment are dry cupping over the loins, warm baths, if the patient's condition permits, and digitalin $\frac{1}{100}$ gr. injected hypodermically.

General measures of treatment should include rest in bed even in mild cases, hot bottles to the feet and limbs, and massage to relieve the cramps. Adrenalin and pituitary extract given by injection have also been recommended.

The diet should be only water, or barley water, during the acute stages. Great care should be exercised to avoid increasing the diet too suddenly. Whey, milk, farinaceous or Benger's food, and custards should be given at first. Soups and meat extracts should not be given until the kidneys are acting satisfactorily. The diet may then be gradually increased. Alcohol should not be given during the acute stage but is useful during convalescence. Tonics and change of air are usually necessary to complete recovery.

In the treatment of cholera cases it is advisable, if possible, to have a separate room set apart for giving injections, with a concrete or other impermeable floor, and as an emergency method the floor may be covered with tin, as was done in Mesopotamia. Certain medical units or portions of units should always be set apart for the treatment of cholera cases, and their location communicated to all concerned. These units should as far as possible be especially equipped for the purpose, and endeavour should be made to staff them with medical officers and subordinates with practical experience of the treatment of the disease.

Prevention.

With regard to preventive inoculation, there can be no doubt that inoculation with a cholera vaccine has an influence in protecting against the introduction of the disease, and it may also succeed in rendering it milder should it occur, although the following statistics, which were collected by Willcox in Mesopotamia, appear to show that the value of inoculation in reducing the case mortality is doubtful.

	Cases of Cholera.	Deaths.	Percentage.
British—			
Inoculated	56	20	35·0
Not Inoculated	27	18	46·0
Unknown	54	31	57·4
Indian—			
Inoculated	122	36	29·6
Not Inoculated	71	22	31·0
Unknown	246	90	36·6

The following table shows the state of inoculation in all the cases which occurred in Sinai.

	Total No.	Fully Protected.*	Partly Protected.	Unknown.
Cases	28	8	16	4
Deaths	7	1	2	4

*Fully Protected=2 injections of cholera vaccine within four months.

No information is, however, available to show the degree of protection that had been obtained or the strength of the vaccine used.

Unfortunately, the period of protection is comparatively short and marked immunity does not last for more than three months. It is highly advisable, nevertheless, for every person to be inoculated against cholera, if there is any possibility of the disease occurring. Still more is it necessary if the disease prevails in epidemic form, or if a visit has to be paid to an endemic area during the seasonal prevalence of the disease, or in war if it is known to be prevalent among enemy troops. Both in Mesopotamia and Egypt, where cholera occurred, prophylactic inoculation was carried out on a large scale and a high percentage of inoculation secured among both British and Indian troops. It was observed, however, during the war, that the vaccines which were used at first did not give a sufficiently high protection, so that in the later vaccines the dose of cholera bacilli was increased. The earlier vaccines contained 500 million cholera bacilli to the c.c. This strength was increased to 1,000 millions, to 4,000, then 5,000, and subsequently to 10,000 millions per c.c. which was given in two doses at intervals of seven to ten days, the first dose being ½ c.c. and the second 1 c.c.

Native followers, and wherever possible the civil population, should also be protected by inoculation. In stations or districts where cholera recurs yearly, it would be a wise precaution to cause the inhabitants to be inoculated annually, shortly before the probable time of the appearance of the disease. As the constitutional and local reactions following the injection of anti-cholera vaccine are generally slight, there ought to be no objection to this measure.

During the war, in addition to the areas, Mesopotamia and Sinai, in which cholera actually occurred among the troops, anti-cholera inoculation was carried out on a large scale on the Salonika front, so that by the end of March 1915, in a large proportion of the units, 90 per cent. of officers and men were inoculated.

The preventive measures adopted against cholera in France, Salonika, Mesopotamia and Sinai were briefly as follows.

In France in 1915 comprehensive preventive preparations were made in view of the fact that cholera was reported to have broken out in the German army and might at any time be introduced into the British force. All units were asked to send in the names of officers and other personnel who had experience of cholera. Certain field ambulances and other units were detailed to organize small cholera sections, to be opened for the reception of cases at a moment's notice. Cholera equipment with a reserve of stores was sent out from England and held in readiness at the Base Depots of Medical Stores at Boulogne, Calais and Rouen for despatch to the medical units.

The following simple pamphlet on preventive measures was printed and issued to the troops.

> "*CHOLERA.*
>
> 1. The *only* way in which you can get cholera is by swallowing the germs. It is not "contagious" or "catching."
> 2. When cholera germs are passed in the fæces or vomit of a man suffering from the disease they may get into water or on the food, which thus become infected.
> 3. In the great majority of cases infection is caused by drinking infected water or swallowing infected food.
> 4. The cholera germ is one which is very easily destroyed by heat, and any suspected water or food can be made perfectly safe by boiling or thorough cooking, especially if such food is kept protected from flies.
> 5. There is very little danger if you remember the following things :—
>
> *Don't drink* any unauthorized water or milk unless it has been boiled.
> *Don't eat* uncooked fruit or vegetables, or any food which has been exposed to flies.
> *Don't drug* yourself with opening medicines, which may make you more liable to an attack.
> *Don't wait* if you have a slight attack of diarrhœa, but report at once to the medical officer.
> *Don't worry.* If you think you have it, you are probably wrong and, if you prove to be right, worry lessens the excellent chance given by the prompt treatment you will receive."

In Salonika, the D.M.S. of the British army was kept informed of the prevalence of cholera by the representatives of the International Commission of Hygiene. It was stated at one meeting in January 1916, that a type of enteritis resembling cholera was fairly common in the Salonika area, and in March true cholera was reported amongst the Serbians at Corfu, while a number of cases were reported to have occurred in the Bulgarian Army. Measures were at once taken to prevent the spread of cholera from the Serbians at Corfu, from captured Bulgarian prisoners of war, and from refugees from Asia Minor to the British force. The French established disinfection stations at Mikra Bay, and the Serbian Army was inoculated with cholera vaccine.

During April and May 1916, the D.M.S. selected special medical units for the treatment of cholera cases in the 12th Corps area, the 16th Corps area, the Mounted Brigade Stavros area, the Base area and Lembet area. The units were equipped with cholera outfits and organized cholera compounds were formed inside barbed wire enclosures. Special incinerators, drinking water tanks, food safes, tub disinfectors and latrines and ablution places were erected, and detailed instructions issued regarding contacts, disinfection of quarters and other preventive measures. The pamphlet, which described in simple language what individuals should not do and which was first published in France, was issued to the troops. Certain field ambulances in the forward area were also equipped with cholera outfits and organized small cholera units. A leaflet on the value of cholera inoculation was circulated, but, having due regard to the primary importance of protecting the troops against typhoid and paratyphoid, anti-cholera inoculation was only pressed after a T.A.B inoculation had been carried out.

Prisoners of war were disinfected, isolated and examined by a medical officer daily for seven days.

During June, July and September 1916, suspected cases of cholera were reported from Kuskus in the 5th Mountain Battery, the 81st and 83rd Field Ambulances, and in the 10th Devons. All these cases were examined for the cholera vibrio, but were found to be negative.

Preventive measures were continued during 1917 and 1918 and No. 7 Base Depôt Medical Stores was ordered to keep in reserve from existing stock 20,000 doses of cholera vaccine, which were not to be issued for routine inoculation but kept for an emergency. Between May and August 1917, 190,000 double doses of cholera vaccine were issued to medical units.

In Mesopotamia when the cholera epidemic commenced the following special measures were ordered.

Certain medical units were reserved for cholera cases. A large number of diarrhœa cases was examined and it was found that 33 per cent. of the cases which had been diagnosed "diarrhœa" were really cholera cases. These cases were admitted to special hospitals.

Convalescents and contacts were collected in camps at Sheikh-Saad, Amara and Basrah. These camps were rapidly filled and it was necessary to consider what constituted a cholera contact. The following circular memorandum regarding cholera was issued as a guide on 13th June, 1916.

"(*a*) During the present cholera outbreak it has been shown that a high proportion of persons suffering from severe diarrhœa harbour cholera vibrios. Complete action to remove this 'carrier' danger cannot be taken but the following partial action is suggested:—

(i) Every hospital should set apart a certain number of wards or tents in which all cases of diarrhœa should be treated apart from the general cases, and with separate latrine arrangements.

(ii) In regiments and other units (when it is practicable to do so) men who have diarrhœa but are still able to do their duty should be accommodated separately from the rest of the regiment and should have separate latrine accommodation.

"(*b*) It has been found that almost no case of cholera has occurred among the very large number of 'contacts' segregated in accordance with the usual procedure. This justifies the modern view that segregation of contacts in separate contact camps is unnecessary. The action advised is that except in special circumstances only the direct or immediate 'contact' of a convalescent should be removed to a contact camp. By the 'direct or immediate contact' is meant the one or two who were in attendance on the patient before he was seen by a medical officer. If the medical officer of a regiment considers it advisable, this procedure may be supplemented by such measures of segregation of the associates of a cholera patient as may be possible under regimental arrangements. The period of segregation of contacts must not exceed seven days from the occurrence of the case.

"(*c*) The procedure as regards cholera convalescents is that they are to be kept segregated for six weeks after the stools have become normal. At the end of that period, if they are otherwise fit, they are to be returned to duty, only those convalescents who are not fit after the six weeks' period of segregation being invalided to India."

Infectious disease officers were appointed at the front, at Amara, at Ashar and at Basrah. Their duties were to inspect the infected units, to control the measures in the infected areas, to arrange for immediate notification of cases and their removal together with the contacts, to carry out disinfection and inoculation, and to supervise the water supply and conservancy. These officers had also to deal with the civil population, among whom the disease was prevalent.

Eleven cholera outfits were dispatched from Egypt on 26th April. Twenty-eight were dispatched from London on 13th May, and twenty-six special water testing outfits for cholera were sent out at a later day.

From 1st to 21st May, 1916, 150,000 c.cs. anti-cholera vaccine were sent from India, and the prophylactic inoculation against cholera was commenced in all formations. Administrative medical officers were instructed to carry out anti-cholera inoculation in the following manner. ½ c.c. and 1 c.c. of anti-cholera vaccine were to be given at an interval of 10 days and re-inoculation carried out at intervals of three months during the subsequent cholera seasons. A record of these inoculations was entered in the soldier's pay book. It was arranged that India should supply 5,000 c.cs. of anti-cholera vaccine weekly.

In Sinai very complete preparations were made in anticipation of the possible occurrence of the disease among British troops. These included anti-cholera inoculation on a large scale of all officers and men who had not been inoculated within three months, together with special arrangements for dealing with captured enemy forces. Intelligence officers gave special attention to information regarding sickness in enemy formations and areas, and information was obtained indicating the probable presence of cases of cholera among the Turkish troops at Katia and Bir-el-Abd in the Sinai desert.

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CHAPTER V.

TYPHUS FEVER.

THE story of the dire results of typhus is written in the darkest pages of human history. True to its traditions typhus appeared, in the first six months of the war, in the Balkans and the Eastern war areas, and subsequently in nearly all the countries and areas in Europe affected by the war, with the notable exception of France, Belgium and Italy.

Its scourges have exceeded those of any other epidemic disease during the war, and it has persisted in the Russian, Polish, and to a less extent in other Eastern War Areas, so that its prevention presents for solution the most difficult problem in epidemic disease which the war has left as its heritage. So widespread has been its extent, so severe its ravages, that even now accurate data about it are still wanting.

The most reliable data were procured from the British Government's Sanitary Mission to Serbia. The Serbian Government appealed for help to the British Foreign Office on 9th February, 1915, and six days later Colonel W. Hunter, A.M.S. (T.F.), the Senior Physician of the London Fever Hospital, with Lieutenant-Colonel G. E. F. Stammers, R.A.M.C., as sanitary officer, Captain W. W. C. Topley, R.A.M.C., as bacteriologist, and twenty-two lieutenants of the Royal Army Medical Corps, left for Serbia in charge of the unit, with instructions that the Mission was not to be employed in hospital clinical work, but should, after ascertaining the actual prevailing conditions and character of the epidemic, form some definite programme to prevent and check the epidemic in the Serbian armies and throughout the country. The Mission arrived at Nish on 4th March, 1915, when the epidemic was increasing by leaps and bounds.

Ætiology.

Till 1870, typhus was more or less endemic, and in some cases even prevalent in most of the countries of Europe. Since then and until the war broke out in 1914, it had become an almost unknown disease. The information obtained of its ætiology and lice-borne mode of infection during the war, exceeded that obtained during the whole previous history of the disease. Overcrowding in houses, malnutrition and squalor were well-known ætiological factors, but they are quite subordinate to the infection carried by lice from person to person, as first described by Nicolle in 1902. The infection is conveyed chiefly by bites, but experiments during the war proved the possibility of the transmission of typhus by the excrement of infected lice being rubbed into scratches or abrasions. Lice multiply rapidly, producing 70 to 80 eggs at a time; the eggs reach maturity in about 17 days, so that a couple of lice in one month can give birth to more than a thousand. Lice cannot travel more than 100 metres, but within their radius they move about very freely. They live on human blood, and when deprived of it, die in two to five days. It suffices, therefore, to leave uninhabited for two to three weeks a house which is infested with lice, in order to free it from any possibility of typhus infection. The proportion of lice which become infected is not known. The life-cycle of the infection is five days' incubation in the louse and ten to twelve days' incubation in man. Until it was clearly ascertained that lice were the carriers, typhus had always been regarded as pre-eminently the disease of overcrowding, and the remedy was "let the crowds of inhabitants be scattered," the rule laid down by one of the chief observers during the great Irish famine of 1847. The rôle of overcrowding and its concomitant factors were subsequently made clear. They contribute to the spread of typhus by favouring the prevalence of lousiness, the number of infected lice, and the spread of such lice from person to person.

Distribution.

Up to the outbreak of the Serbian epidemic there was no previous experience in utilizing this knowledge to check the disease when in epidemic form. The only information on the point was obtained from Nicolle, who succeeded in reducing the number of cases in Tunis, where typhus was endemic, from 836 cases in 1909 to 3 cases in 1914 by the disinfection of all infected personnel, clothing, bedding and rooms.

The British troops, although operating in areas where the disease was endemic, and in contact with infected allies and enemy, suffered little from typhus, and our knowledge of the disease is principally derived from the work of Colonel Hunter's mission during the epidemic in Serbia. The information from other countries is necessarily scanty, only enabling approximate figures to be given, but it shows that the spread of the disease may be traced from Russia, Russian Poland, Austrian Galicia and Styria, and Turkey to the Balkans and Europe.

There is no doubt that Russian prisoners conveyed typhus to Germany and Austria. The number of cases in Russia is unknown, and will doubtless never be known. It is estimated at ten million with two million deaths. The Russian territories and armies have, in fact, been the chief seat and source of the spread of the disease throughout the war.

In Russian Poland the average annual number of cases prior to 1914 was 1,887. The Germans overran this country in 1914 and are reported to have suffered difficulties from, and taken great precautions against, typhus. A severe epidemic occurred in the latter part of 1916 and again in November 1917, when 26,099 persons were attacked by the disease in the Warsaw district. The mortality was very low, being only eight per cent. The total number of cases in Poland during the war has been estimated at 400,000 with a mortality of 10 per cent., but the figures are probably underestimated.

Typhus is endemic in Turkey, and there was a widespread development of the disease in and around Constantinople and in all the provinces, especially in Palestine and Armenia. One epidemic among the soldiers of the Van population showed 4,500 cases. Of this number 19 officers and 2,690 men died, a mortality of 50 per cent.

In Austria, typhus, in addition to being endemic in certain areas, broke out in 1914 in a camp containing 9,000 Russian prisoners, and 300 cases were reported in less than a week. In January 1915, 1,500 cases, including 1,000 from Styria, were notified, and in the following month another outbreak occurred in a Russian prisoners' camp, followed by a severe epidemic in Przemyśl, Galicia.

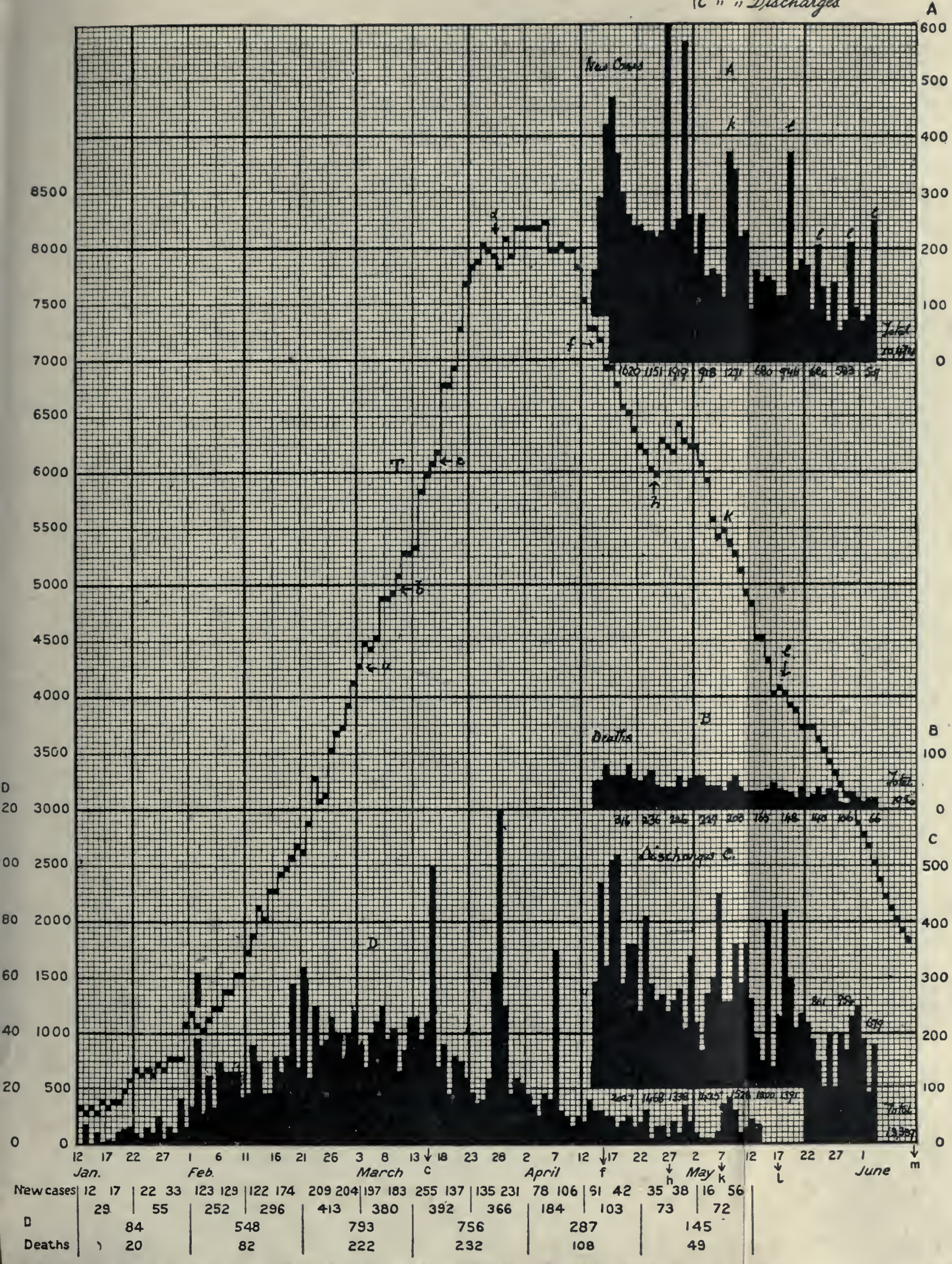
The presence of typhus in Turkey and Austria was an important factor in causing the 1914–1915 Serbian epidemic. The southern part of Serbia had been under the Turk for five hundred years, but, as the result of the Balkan War in 1913, it had come into the possession of the Serbs. In common with all areas governed by the Turk, this southern area was the endemic seat of typhus, and in 1913, 100 cases were reported in Belgrade. In Austria, the disease always remained endemic, especially in Galicia and Styria. The Austrians by employing troops from these areas spread the infection to other areas. The chief extension was caused by the Austrian invasion of Serbia in 1914. The Serbian army had been quite free from typhus, and when the Serbs retreated in November 1914 from Valyevo, a town near the Bosnian frontier, they left it free from typhus. On recapturing Valyevo and during the advance, they took about 40,000 prisoners and 3,000 sick and wounded. The Austrians had left many of their sick and wounded who were suffering from typhus in Valyevo, and many of their dead were left unburied in the cellars or only partially covered with a foot of soil. The prisoners were distributed over the country partly from lack of accommodation, and partly from need of their labour. The infected prisoners thus spread the disease broadcast through the Serbian troops to the civilian population. The great Serbian epidemic followed. It commenced in December, gained head in January, and broke out over the whole country in greatest intensity during February and March 1915. Under more favourable circumstances, greater attempts might have been made to concentrate these prisoners and establish some measure of quarantine before dispersing them throughout the country, but the small and exhausted forces of the Serbians and the impoverished conditions of the country did not permit of these precautions being taken. The Serbs had neither accommodation nor food for idle prisoners in camp. They had not troops to guard the prisoners, and the need for their labour in the country was pressing.

The outbreak was of the severest character and widest extent ; it raged through every town, village and hamlet in the land, finding conditions extremely favourable to its spread. By the end of December 1914, 100 cases were reported, and by the end of January 1915, 1,100 cases. Thereafter the course of the epidemic was fulminating, very imperfectly represented by the official figures of cases in hospitals, for the sufferers numbered thousands and the hospitals were few and quite inadequate for their accommodation. On 28th February those in hospitals were over 3,000 and the mortality was 30 per cent. By 31st March the number had risen to 8,200 and a mortality of 60 per cent. was not unknown. These figures represent very imperfectly the widespread character of the epidemic among the civilian population in villages, where the proportion of sufferers was probably five to one of the military patients. Estimates of the total number of deaths caused by the epidemic range from 100,000 to 135,000, including two-thirds or more of the 40,000 Austrian prisoners. To the credit of the Serbian authorities, the very limited and utterly inadequate hospital accommodation was shared impartially by prisoners and their own soldiers. But the overcrowded and squalid conditions under which the prisoners lived, worked and slept greatly favoured the chance of infection, and led to a correspondingly greater prevalence of the disease among them. Observers working in such an epidemic realized something of the terrible fate which befell those who were stricken by this dread disease.

In the case of Serbia the epidemic was immediately arrested by the preventive measures put in force on 16th March, 1915, eleven days after the arrival of the British Sanitary Mission. Its enquiry into the origin and subsequent distribution of the

To face page 136.

Chart I Course of Epidemic of Typhus in Serbia in 1915, as shewn by
T No. of Cases in Hospital
A " " New Cases (April 17-June 4)
B " " Deaths
C " " Discharges



D= Daily Admissions of Typhus in 1st Reserve Hosp. Kragujevatz

COURSE OF EPIDEMIC OF TYPHUS FEVER IN SERBIA, 1915, AND ITS RELATION TO PREVENTIVE MEASURES ADOPTED.

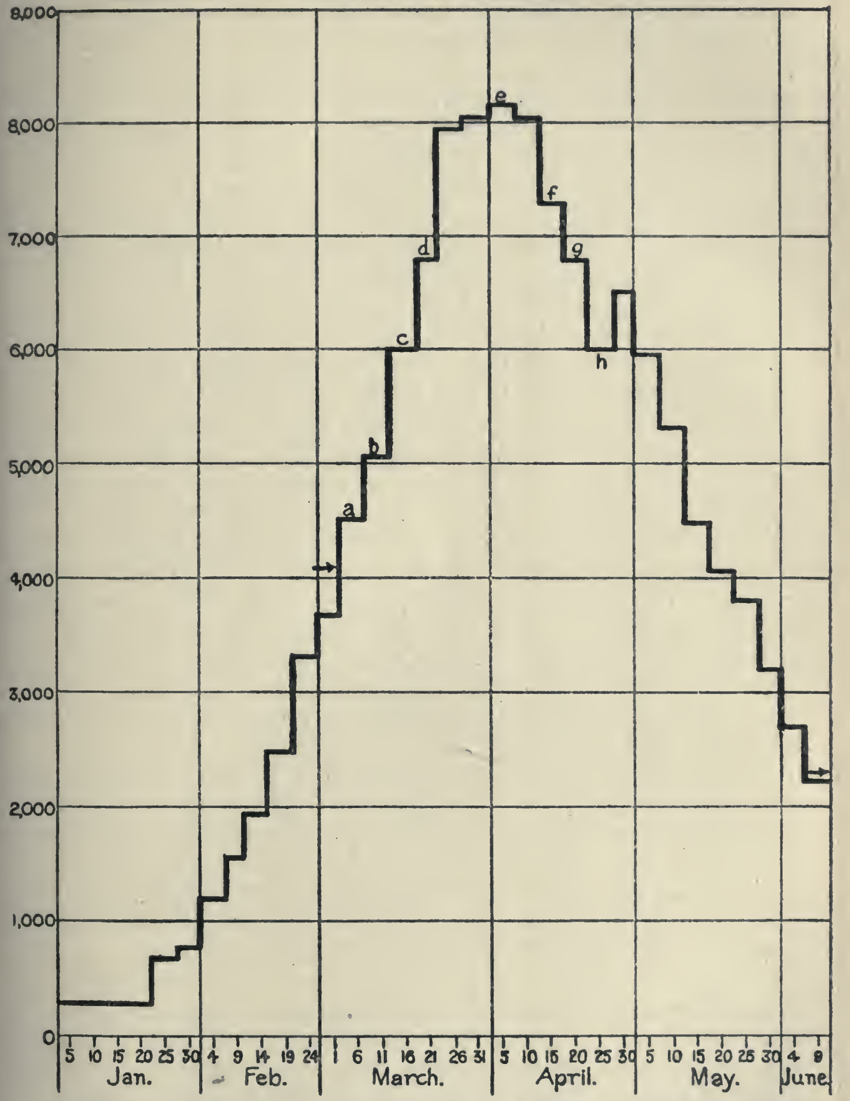


CHART II.—Number of cases of typhus in hospital in Serbia on dates specified, January 1 to June 9, 1915.

March 4.—Arrival of Mission in Serbia. June 10.—Departure of Mission from Serbia. *a*, March 8.—Barrel disinfector devised. *b*, March 13.—Barrel disinfector made and tested. *c*, March 15.—Suspension of railway traffic. *d*, March 22.—Van disinfector devised ("Van 1"). *e*, April 5.—Van disinfector ("Van 2") formed in Nish; van bath devised. *f*, April 15.—Resumption of railway traffic. *g*, April 19.—English sanitary train (inoculation, disinfection and bath vans). *h*, April 25-30.—Sudden check in fall of epidemic ten to fourteen days after the resumption of railway traffic.

typhus epidemic showed that the army areas in the north were chiefly affected, 49 per cent. of the cases in hospital being in these areas, and only 28 per cent. in the southern civilian areas. The infection had thus been introduced specially into the armies and thence to the civilian areas. Accordingly two great preventive measures, suspension of all railway traffic and stoppage of all leave from the army combined with delousing, were put in force on 16th March, 1915, and within ten to fourteen days (the incubation period of the disease) the number of patients in hospital reached its maximum. The number of new cases was reduced to one-half in two weeks, and one-fifth in four weeks. The number of daily admissions to the whole of the hospitals decreased from 1,500 cases on March 16th to 230 cases on April 16th, and 100 by May 31st. The epidemic was so completely arrested in a month's time that by the middle of April movements of troops began again, and, although this caused a slight temporary increase in the number of cases admitted to hospital, the epidemic could be reported at an end by May 17th, and the British mission was consequently recalled on June 1st.

If an epidemic can be said to have a useful purpose, this epidemic was probably useful in two ways. It gave the Serbians, exhausted as they were by their military efforts, complete military peace for nine months, since the fear of entering a country infected by typhus may have deterred the Austrians, Germans and Bulgarians from attack; and it demonstrated the striking effect of preventive measures when applied simultaneously to the whole country.

The subsequent incidence of typhus in Serbia is interesting. Apart from an article in the German press in 1916 by Dorendorff, who gives his observations on a limited epidemic of typhus which had broken out among the troops operating in Serbia, no definite information is available concerning the regions occupied by the Austrians, Germans and Bulgarians from November 1915, to October 1918. It is known, however, that although the Serbian army in its retreat lost thousands and tens of thousands from exposure, diarrhœa and starvation, it had only a few deaths from typhus, owing to the use of the barrel disinfectors introduced into Serbia by the British Mission, and, in May 1916, arrived 150,000 strong in Salonika, developing only three or four cases of typhus on the voyage from Durazzo and Corfu to Salonika.

Typhus from 1892 to the outbreak of the war was practically non-existent in Germany, but exact data from 1914 onward are not known. The Germans had difficulties in Poland in 1914, and early in 1915 reports were received that the diseas had broken out in prisoners' camps—Hamburg, Wittenberg and Gardelegen. In Gardelegen there were 12,000, chiefly Russian and French prisoners, with 1,000 Belgian and 230 British. A historic report on this camp was published by Major P. C. T. Davy and Captain A. J. Brown of the R.A.M C. In the Wittenberg camp the epidemic raged for the first six months of 1915. There were between 250 and 300 cases among the British prisoners, of whom 60 died. The mortality amongst the French and Russians was very much higher. A full report was written by Major Priestly, Captains Vidal and Lauder, all of the R.A.M.C., and all prisoners of war. The conditions which existed in these camps form the most appalling reading connected with the history of typhus in prisoners' camps during the war.

A certain number of cases was reported in Greece in 1914, but the Greek authorities, being alive to the necessity of preventive measures, applied them with such success that only 200 cases occurred in Salonika during the period of the Serbian epidemic.

A mild epidemic broke out in Bucharest during the latter part of 1915 and early in 1916. From January to June 1917, a severe epidemic attended with a high mortality raged in Moldavia.

With regard to the incidence of typhus in the British Armies, in Gallipoli there were no cases. In Salonika from 1916 to 1918 there were no cases; but subsequently in 1919 five cases occurred. During 1919 and 1920, 17 and 12 cases respectively were reported from the army of the Black Sea, with six deaths, a mortality of 27·6 per cent. In Egypt and Palestine there were 22 cases during 1916–1917, when the troops were for the most part in Egyptian territory, and 344 cases in 1918–1919 when they conquered and occupied Palestine. The number of deaths was 80, or a mortality of 21·8 per cent. In Mesopotamia the infection spread to British troops from Turkish prisoners of war, Arabs and refugees; during 1917 and 1918 there were 385 cases amongst the Indian troops, with 149 cases amongst the British troops and 59 cases in 1919. The mortality was 22·7 per cent.

In France and Italy there were only five cases. Preventive measures are responsible for the freedom from the disease testified by these figures, notwithstanding the prevalence of lice and the risk of infection from Egypt and Portugal.

Typhus broke out in Oporto in March 1918, and from May to November 1,811 cases are stated to have occurred in Portugal, so that the risk of its introduction into the armies in France through the Portuguese contingent was very great.

Altogether the total number of typhus cases among the British forces in all war areas was 998, of which 221 were fatal. Their distribution is shown in the following table :—

Incidence of Typhus in British War Areas, 1916–1920.

	1916		1917		1918		1919		1920		Total.		
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Case Mortality.
France	4	–	1	–	–	–	–	–	–	–	5	–	–
Egypt	10	2	12	4	208	51	136	23	–	–	366	80	21·8%
Mesopotamia :—													
British	–	–	11	7	138	27	59	12	–	–	593	135	22·4%
Indian	–	–	8	4	377	85	–		–	–			
Army of Black Sea ..	–	–	–	–	–	–	17	2	12	4	29	6	20·6%
Salonika	–	–	–	–	–	–	5		–	–	5	–	–
Total Cases ..	14	2	32	15	723	163	217	37	12	4	998	221	22·1%

The chief incidence of the cases in Egypt and Palestine was between January and June, reaching its height in April, as is shown in the following table :—

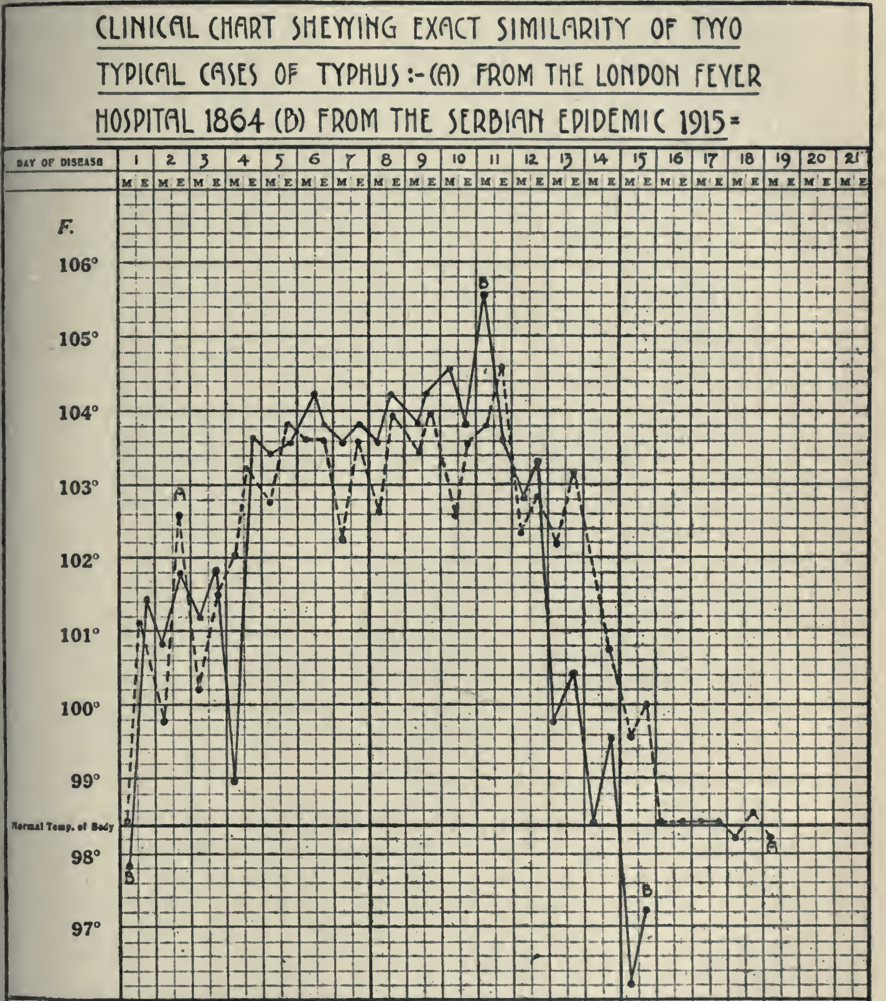
Monthly Incidence of Typhus in British Troops in Egypt and Palestine, 1916–1919.

Month.	1916	1917	1918	1919	Total.
January	—	—	25	16	41
February	—	2	21	12	35
March	1	4	43	21	69
April	4	2	47	23	76
May	2	2	37	17	58
June	1	1	19	40	61
July	1	1	7	2	11
August	—	—	2	—	2
September	—	—	1	3	4
October	—	—	6	2	8
November	—	—	—	—	—
December	1	—	—	—	1
Total	10	12	208	136	366

So far as is known there were no cases in the French, Belgian, and Italian armies, but 3,321 cases occurred in a camp for Austrian prisoners in Italy during 1919.

Symptoms.

The incubation period of the disease is from 10 to 12 days. Most observers consider it to be about 10 days ; Murchison fixed it in the majority of cases as not more than 12 days. These results were confirmed and strikingly demonstrated by the course of the Serbian epidemic, by the arrest of the disease within fourteen days of the suspension of railway traffic on March 16th, and by its temporary recrudescence exactly fourteen days after the resumption of traffic on April 16th.



CLINICAL CHART SHEWING EXACT SIMILARITY OF TWO TYPICAL CASES OF TYPHUS:-(A) FROM THE LONDON FEVER HOSPITAL 1864 (B) FROM THE SERBIAN EPIDEMIC 1915=

			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
CASE A	PULSE	Morning	80	90	100	104	108	112	120	112	124	116	116	108	96	88	98	68	68	50			
		Evening	90	100	100	108	110	116	124	128	122	120	116	100	92	78	68	68	52	68			
CASE B	PULSE	Morning	92	94	100	90	118	110	108	108	110	110	140	120	110	90	80	70					
		Evening	94	100	104	116	110	112	115	116	118	120	140	116	100	94	66	60					

CHART III.

The clinical features of typhus are those of a severe toxic disease, affecting specially the brain and the heart. The course of the disease is very definite, extending from first to last over a period of two weeks, divided into four stages of approximately four days each :—(*a*) the stage of invasion (three days) ; (*b*) the stage of advance (four days), commencing with the appearance of the rash and ending with prostration, sleeplessness, restlessness and delirium ; (*c*) the further stage of advance (five days), marked by increase of all the symptoms, especially of delirium and heart weakness, until on the twelfth day the patient is in a critical condition ; (*d*) the stage of crisis about the twelfth or fourteenth day, when the whole symptoms suddenly ameliorate by a sharp crisis or by rapid lysis, fall in temperature and return to normal pulse in the course of two or four days. The patient who, delirious and unconscious, has been at death's door on the twelfth day recovers so quickly that he may be able to get up by the sixteenth day and leave the hospital by the twentieth day, completely recovered though still weak. The course of the disease from first to last is represented on the preceding chart of two cases, one taken from the records of the London Fever Hospital, 1864, described by Murchison ; the other from the Serbian epidemic, 1915, described by Minkine. The close similarity between the two curves is remarkable, and extends to all features. A detailed comparison of the symptoms presented in cases in the Serbian epidemic with those classically described by Murchison in the 20,000 cases in the London Fever Hospital, 1848 to 1870, shows that the former were almost identical with those already known, differing, if at all, only in their severity, their greater number, and the distressing circumstances of their surroundings.

Diagnosis

The diagnosis presents little difficulty when typhus occurs in epidemic form, but it is otherwise when met with sporadically by those, and they include the great majority of medical officers, who have never seen a case before. The appearance of the rash on the fourth day distinguishes it from influenza, while the absence of rash from the face and neck and its discreet nature eliminate measles. Relapsing fever is unaccompanied by a rash and the spirillum can always be discovered in the blood on the third or fourth day. Typhoid and the paratyphoids are diagnosed by the isolation of the typhoid and paratyphoid organism. Cases of meningitis show intolerance to light and sun, whereas the typhus patient is indifferent to both. Difficulty in diagnosis is diminished by the use of the Weil-Felix agglutination test with the organism *Proteus X*.

Prognosis.

The prognosis is always grave and is influenced by the nervous disposition of the patient. A strong healthy young officer, who from his previous knowledge dreads the disease, may succumb; while the exhausted peasant soldier, worn out by over-exertion and under-feeding, recovers. This probably explains the high mortality amongst the Serbian doctors who were stricken down by typhus. Out of a total of 450, at least 360 were attacked and over 120 died. In an epidemic under the conditions of poverty, stress and misery, there is no disease except cholera and plague comparable with it in danger to every patient attacked, or to the attendants who nurse them. When the disease is epidemic and virulent, the certainty is that nearly a third of the patients will die, and at the height of an epidemic the proportion may rise to one-half, as is shown in the following table:—

Figures from the largest Fever Hospital in Serbia—(Kragujevatz), 1st January, 1915—13th May, 1915.

Date.	No. of Days.	Admissions.	Average Daily.	Completed Cases.	Deaths	Mortality on Completed Cases.
January 1—11	10	34	4	--	—	—
January 12—21	10	29	3	—	—	—
January 22—31	10	55	5	—	21	—
February 1—10	10	252	25	—	—	—
February 11—20	10	296	29	—	—	—
February 21—March 2	10	413	41	700	185	30·0%
March 3—12	10	380	38	200	119	59·0%
March 13—22	10	390	39	—	124	—
March 23—April 1	10	366	36	—	88	30·5%
April 2—11	10	184	18	—	63	32·0%
April 12—21	10	103	10	—	45	17·4%
April 22—May 1	10	73	7	—	23	—
May 2—12	10	72	7	—	26	14·4%
Total	130	2,647	20·1	900	694	30·4%

Treatment and Prevention.

With regard to treatment, sera have been tried with indifferent success, and Murchison's dictum still remains true: "A patient with typhus is like a ship in a storm; neither the physician nor the pilot can quell the storm, but by tact, knowledge, and able assistance they may save the ship."

The measures of prevention are themselves simple in character, easily applied, and are directed against lice on clothes and persons; but the difficulties in applying the delousing measures on the scale and with the frequency required, owing to the prevalence of lice in armies numbering millions, have been enormous and have taxed to the full the efforts and the medical resources of the armies concerned.

The allied armies with the exception of the Russian were successful in combating the disease. The preventive measures adopted in Russia were either too limited or broke down. In Serbia the education of the people by means of pamphlets and appeals issued by the British mission within three days of its arrival, the isolation of cases, the segregation of contacts, the suspension of railway traffic both for the movement of troops and for civilians, the opening of bathing and delousing centres, the use of barrel disinfectors designed first by Lieut.-Col. Stammers, steam disinfecting railway vans, railway van douche baths first designed by Colonel Hunter, the formation of British sanitary disinfecting trains, and the cleansing of railway stations and rolling stock, proved successful. The most important of all these measures was the suspension of railway traffic amongst civilians. It was chiefly responsible for arresting the course of the epidemic in four weeks, and, on the restriction being rescinded, a sharp recrudescence broke out and the admission rate to hospital increased three-fold and in some areas eight-fold. In connection with the prevention of typhus the experience of the British mission in Serbia may be summed up as follows :—Prevent all movements of the infected population, and disinfest them in the areas in which they are found, and discard the rule to " Let the crowds of inhabitants be scattered," which in all previous great epidemics was laid down as the chief measure required.

The above precautions were applied in France in connection with the Portuguese troops, when drafts were stopped and afterwards collected, detained in Portugal for 12 days and deloused in an area away from the centre of infection. On arrival in France special arrangements were made for the placing of the troops in quarantine for 11 days at the port of disembarkation, where they again underwent disinfestation before being sent to the front area. On the Eastern fronts these precautions combined with the bathing and delousing schemes in operation in all armies, assisted in procuring the immunity which the British troops enjoyed during the war.

With regard to the precautions taken by the enemy forces, the arrangements made by Austria and Turkey do not seem to have been sufficient, and their armies became severely infected. In the case of Germany, the measures seem to have been a matter of meticulous preparation. They included delousing measures and the supply of appliances on an elaborate scale. In 1913, for example, 250 tons of sabadilla seeds were shipped from La Guaira to Germany; and subsequent instructions were issued by the German Imperial Board regarding the use of these seeds, the active principle of which is veratrine, as a parasiticide. No data of the results of the German preventive measures are as yet available, but considering the dangers to which their armies were exposed, the measures were in all probability successful. Nevertheless, the amount of typhus in the German armies was considerable. Official information furnished up to the end of 1916 gave the number of deaths from typhus as 448. This represents an occurrence of approximately 4,000 cases, which probably extended to all ranks and was prevalent in various camps. When the German armies advanced far into Russia during 1917 and 1918, there is evidence that their measures were relatively successful, because during the period they were in charge of the Warsaw district, the incidence of typhus was held in check, becoming much more widespread after their departure.

The important lesson gleaned from a study of typhus in this war is the necessity for providing simple methods of disinfection available for the smallest companies; mobile disinfecting plant, especially train disinfectors, which can always be in touch with the troops; and a sufficient number of units adequately equipped for delousing in the field not only an army's own soldiers, but also enemy prisoners of war. As armies advance into a country where typhus is known to be endemic, such units, if used to advantage, will play a most important part in preventing the spread of the disease in epidemic form.

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CHAPTER VI.

CEREBRO-SPINAL FEVER.

CEREBRO-SPINAL fever is an infection characterized by meningitis and caused by the *Diplococcus intracellularis* of Weichselbaum. Since its recognition in 1805, the disease has occurred in epidemic waves of three or four years' duration, followed by periods of quiescence. Sporadic cases are always present, and their numbers follow the same seasonal curve as that observed in the larger epidemics. Infants and recruits are peculiarly prone to the disease. In previous campaigns, with the exception of outbreaks in French garrisons during the Napoleonic Wars, and an epidemic in the Army of the Potomac in the American Civil War, the disease has been singularly absent. During the war of 1914–18, however, the disease was epidemic in a formidable manner amongst troops in the United Kingdom, while a concurrent epidemic raged amongst the civilian population, as is shown by the following tables :—

	Troops in the United Kingdom.			Civilian Population.					
				All Ages.			Males 20–30.		
Year.	Cases.	Deaths.	Mortality %	Cases.	Deaths.	Mortality %	Cases.	Deaths.	Mortality %
1914..	46	30	65·2	300	206	68·7	9	4	44·4
1915..	1,199	587	48·8	2,343	1,521	64·9	127	80	63·0
1916..	967	430	44·5	1,278	838	65·6	45	23	51·1
1917..	1,337	593	44·4	1,385	906	65·4	48	31	64·5
1918..	689	288	41·8	715	484	67·6	12	7	58·3
Total	4,238	1,928	45·5	6,021	3,955	65·6	241	145	60·1

Summary.

Population.	Cases.	Deaths.	Mortality Per Cent.
Military	4,238	1,928	45·5
Civilian	6,021	3,955	65·6
Total	10,259	5,883	57·4

The first military case occurred on September 19th, 1914, and somewhat later a serious outbreak took place amongst Canadian troops on Salisbury Plain, among whom cases had already appeared at Val Cartier Camp in Canada, while others had broken out on the voyage. From early in January 1915, the disease became epidemic. As usual, the infection could not be traced from case to case, but occurred in different units scattered throughout the country.

In the British Expeditionary Force in France the disease first appeared in January 1915, and its incidence is shown by the following table :—

Year.	Cases.	Incidence per 1,000 of strength.	Deaths.	Mortality Percentage.
1915 ..	313	·55	—	—
1916 ..	393	·33	138	35·1
1917 ..	701	·43	198	28·2
1918 ..	176	·11	69	39·2

No serious outbreak occurred in any other theatre of war, but cases occurred in the Italian, Mesopotamian and Dardanelles forces, and also amongst the Indians and Arabs in Mesopotamia.*

The seasonal incidence of the disease followed a definite curve, statistics showing that 77 per cent. of the cases in the United Kingdom occurred in the first six months of the year, though no month failed to produce at least one case. From January, the number of cases gradually increased until late March or early April, when a somewhat abrupt decline began. By the end of June only occasional cases occurred. The number of these decreased until December, when it began to rise again.

Ætiology.

Epidemics of cerebro-spinal fever have occurred in most countries in the world, so that climate cannot be claimed as playing any special part in engendering them. Weather conditions, on the other hand, have been accredited with exerting a definite influence on the spread of the disease, which is most rife in winter and early spring. Observations, however, instituted by Sir H. Rolleston at a naval base in 1915, upon northerly or easterly winds, a sudden fall in temperature, and the prevailing wind and average daily temperature contour, failed to show any conclusive relation between these weather conditions and case incidence.

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* A considerable outbreak occurred during 1916–1917 in transports with troops from Australia. From June 1916 to October 1917, 126 cases occurred on transports, the cases and their contacts being landed at Durban or Cape Town. This outbreak is of interest in that, owing to preventive measures employed, the disease did not spread either to the civilian population or to the garrison at the ports at which cases were landed. The measures adopted were segregation of contacts, naso-pharyngeal swabbing of non-contacts to ascertain the carrier rate, and the use of the sulphate of zinc spray in chambers.

Fatigue has been claimed as one of the factors which favour outbreaks of the disease, but no conclusive evidence has been adduced to show that it exerts any more specific influence than other causes of lowered vitality.

No direct relation between previous illness and infection has been established. The pandemic of influenza amongst troops in June and July, 1918, caused no rise in the incidence of cerebro-spinal fever. On the other hand, cases of cerebro-spinal fever complicated by influenza, or *vice versa*, are singularly fatal.

Naso-pharyngeal catarrh has been claimed as a preliminary stage of cerebro-spinal fever. Sophian in America, Lundie, Thomas, Fleming and Maclagan working at Aldershot in 1915, described a catarrhal stage as the first manifestation of the disease. Other observers, Sheffield Neave, Worster Drought and Kennedy, and the Advisory Committee of the Medical Research Committee have failed to substantiate this view, the report of the latter committee pointing out that the only relation is that both diseases occur in winter and early spring. On the other hand, Cleminson's observations show that 50 per cent. of chronic carriers have an excess of adenoid tissue, in whose folds it may be presumed the meningococcus finds a secure nidus. The fact that a chronic carrier can often be entirely cured by the operation of clearing the post-nasal space strengthens Cleminson's contention. Catarrh, therefore, although in no sense increasing the probability of any individual contracting the disease, may, if dependent on abnormal conditions of the mucous membrane, predispose him to become a carrier. Coughing and sneezing may, by increasing the range of his infectivity, tend to widen the spread of an epidemic.

From the study of the recent epidemics, one causative factor stands out with startling distinctness, namely, overcrowding. In 1915, it was at once recognized that wherever cubic space, either in huts or billets, fell below standard, cases began to occur. Captain Glover's work at a depôt in 1917 gives an admirable picture of the mode in which epidemics arise from overcrowding. Glover found that the carrier rate with the peace standard of one yard between the beds rarely exceeded 5 per cent. Mobilization standard of one foot four inches between the beds yielded a carrier rate of 10 per cent. At one foot it rose to 20 per cent, and at less than nine inches 28 to 30 per cent. When the carrier rate rose to 20 per cent. or over, cases began to occur. At this depôt the carrier rate rose as high as 70 per cent. Spacing out produced a fall in the carrier rate, in a slower manner than the preliminary rise.

The exciting cause of cerebro-spinal fever is infection of the meninges by the meningococcus. This is a gram negative organism whose habitat is the vault of the naso-pharynx. Dopter first differentiated this organism into two types, the meningococcus and the parameningococcus, and produced a specific serum for each. By the agglutination test controlled by the absorption test Gordon found that the meningococci of the epidemic during the war were divisible into four types, named I, II, III and IV. Of these I and III correspond to the meningococcus and II and IV to the para-meningococcus of Dopter.

The following table indicates the relative frequency with which the types were found :—

Type	I	II	III	IV
Specimens ..	195	218	69	36
Percentage ..	37·66	44·05	11·38	6·94

Infection spreads from throat to throat and in a small proportion of cases passes inwards from the naso-pharynx and ultimately infects the meninges. Opinions are divided as to whether the infection passes by direct extension through the cribriform plate or through the sphenoidal sinus, or is carried by the blood stream. The occurrence of both rapidly fatal and chronic cases of meningococcal septicæmia, in which the meninges are healthy, are strong arguments in favour of the latter view. Herrick obtained positive blood cultures in the early stages in a large proportion of cases ; other observers met with a contrary experience. Embleton and Peters found meningococci in the pus of the sphenoidal sinus in a large proportion of cases ; but Worster Drought and Kennedy failed to corroborate their observations. It has further been suggested that infection passes by direct extension through the dural sheaths of the olfactory nerves in the cribriform plate. On the whole the view that meningeal infection occurs through the blood stream is most widely held, but definite proof of the actual path is hitherto lacking.

Morbid Anatomy.

With regard to the morbid anatomy of the disease, in septicæmic cases the only appearances to be observed are a hæmorrhagic rash and hæmorrhages on the serous membranes.

Fulminating cases exhibit intense congestion of the cerebral vessels with patches of pus lying in milky exudate. Acute cases dying somewhat later show large plaques of pus scattered over the vertex and covering the base of the brain. The cord is also covered with patches of pus which are most numerous in the dorsal and lumbar region. Microscopically, beyond superficial polymorphonuclear infiltration, there is little pathological change. In a type of chronic case, which usually dies about the third week, the brain and notably the cord are coated with thick shaggy pus, and there is but slight excess of fluid. Cases dying of hydrocephalus exhibit but slight signs of the original infection, pus having disappeared from the vertex and base, while the ventricles are distended with clear fluid. The obstruction will usually be found to be due to matting together of the areolar tissue of the roof of the fourth ventricle. In other cases the iter may be blocked, or adhesions between the spinal and parietal arachnoid may be the cause of obstruction. Changes in other organs are slight. The spleen is not enlarged, the liver and the kidneys show cloudy swelling. The lungs frequently show patches of broncho-pneumonia. The right heart is dilated and pericarditis may rarely be seen. Hæmorrhages into the supra-renal capsules occur with comparative frequency. Death from large retro-peritoneal hæmorrhages has been recorded in a few instances.

Symptoms.

The period of incubation for practical purposes may be regarded as from three to five days. Observations on men returning from leave to a unit hitherto uninfected, as well as observations on carriers who have developed the disease during observation, point to a short period of incubation.

The symptoms of cerebro-spinal fever bear a two-fold aspect, those associated with an infective process, and others due to the evolution of nervous phenomena as the cerebro-spinal system becomes increasingly involved. In a small number of cases the latter class of symptoms may be entirely absent, a meningococcal septicæmia proving fatal while the meninges remain entirely unaffected. Some cases, on the other hand, in which a meningo-coccal infection is proved by positive blood cultures while meningeal symptoms are entirely absent, may run their entire course to complete recovery, exhibiting only the symptoms of continued fever, sometimes combined with a rash or arthritis, or they may, after a long interval, ultimately develop meningitis. With these exceptions, however, cerebral symptoms develop soon after the clinical symptoms of fever.

In the great majority of cases the onset is sudden and generally marked by a rigor, followed by a rise in temperature and marked anorexia. In other cases, the onset may be insidious, malaise and slight headache going on for some days until increased headache and the occurrence of vomiting rouse suspicions of the nature of the malady. In fulminating cases, and in some that recover, the patient passes almost at once into a condition of profound coma. The general aspect is characteristic. In the early stage, the patient presents a flushed face, with an aspect of suffering; sometimes the expression is one of startled apprehension. As the disease progresses, this gives place to a dull heavy look recalling that of typhus. The patient usually lies curled up in bed or may rest face downwards supporting his head with his hands. Headache rapidly follows the initial rigor. This varies in its initial severity and in the rapidity of its exacerbation. As a rule, the whole head is affected; pain may be more pronounced in the frontal or occipital region, but is never unilateral and is rarely influenced by drugs. The severity of the pain steadily increases, and may be of the most agonizing character. A slight degree of photophobia is usually present, but it is not so marked a symptom as in tubercular meningitis. With the exacerbation of the headache, vomiting shortly sets in. This is an almost constant symptom, but usually only lasts for about 24 hours.

Delirium occurs in a large proportion of cases, the date of its onset varying from a few hours to five or six days. It varies from violent, almost maniacal excitement, to mere muttering, and in all its phases constant complaint is made of headache. In acute cases delirium leads on to stupor and this in turn passes into coma.

The temperature usually rises to between 101° and 103°F. after the preliminary rigor, and remains elevated during the course of the acute symptoms. The temperature curve affords no measure of the severity of the disease. The pulse, except in very acute cases, is somewhat slow in relation to the temperature.

In about 50 per cent. of cases, a rash makes its appearance; in fulminating cases, large purpuric spots appear on the body and also involve the face. In acute cases, a petechial rash appears which consists of small papules, varying in size from a pin's head to a peppercorn, and occurring principally on points of pressure, notably the trochanters, knees and elbows, malleoli and points of the shoulders (Plate I, Fig. 2). This rash is seen from the first to the third day, and is always evidence of profound toxæmia. The macular rash (Plate II),

Plate I

Fig. 1.
CEREBRO-SPINAL FEVER—ERYTHEMATOUS RASH.

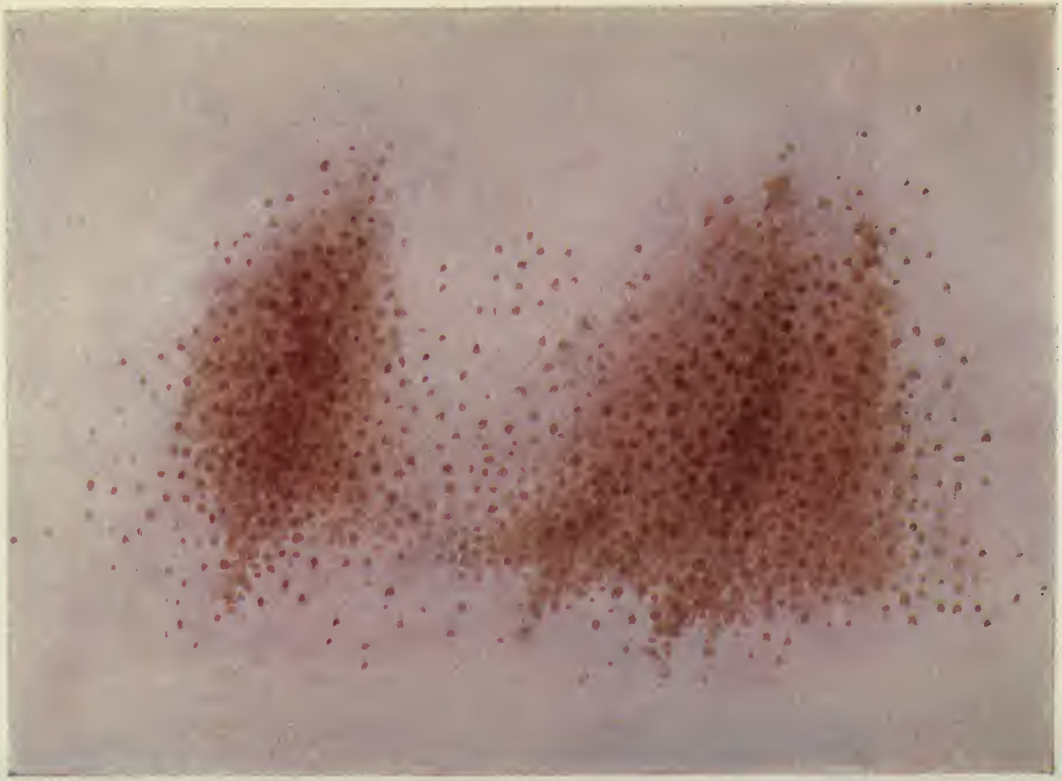


Fig. 2.
CEREBRO-SPINAL FEVER—PETECHIAL RASH.

which may be regarded as the specific rash of the fever, appears on about the fourth day and the distribution affects first the abdomen, then the thighs, the extensor surfaces of the forearm and legs, the back of the hands and the dorsum of the foot. The individual maculæ vary in size from that of a millet seed to that of a No. 1 shot, and in colour from scarlet to purple. A transient erythematous rash may appear at any time during the disease (Plate I, Fig. 1). The larger purpuric spots may undergo ulceration, as pointed out by Elliott and Kaye, who refer to the lowered vitality engendered by cold in the trenches as favouring increased size in the purpuric patches and also a tendency to ulceration (Plate III). In from 30 to 40 per cent. of cases, herpes appears from the third to the sixth day, usually about the fourth. The vesicles are almost invariably facial or auricular in distribution, though other nerve areas such as the lumbar and sacral are occasionally affected.

Of symptoms more directly concerned with the nervous system, one of the earliest to manifest itself is retention of urine ; this occurs in about 50 per cent. of cases, and is not necessarily attended by mental hebetude. This symptom is of considerable diagnostic importance, as in no other febrile malady does retention occur at such an early stage. At later stages of the disease, notably in hydrocephalus, there may be incontinence both of urine and fæces. The febrile onset is often attended by general myalgic pains ; these in turn are succeeded by a varying degree of muscular rigidity. Rigidity and contraction of the muscles of the neck leading to retraction of the head form one of the most striking symptoms of the disease. This sign varies in the date of its appearance, but is usually present on the second or third day. It may, however, be delayed to the fifth or sixth. Few, other than fulminating cases, fail to show this sign at some period of their course. Another form of rigidity which is always manifested is the tonic contraction of the ham-strings which gives rise to Kernig's sign. This phenomenon is present in all except fulminating cases. It usually appears at the end of 18 hours, is fully established at the end of 24, and is of great diagnostic importance. As the disease progresses, other forms of rigidity make their appearance and should hydrocephalus ensue both arms and legs may become rigid and flexed.

The reflexes vary in different cases so that no diagnostic significance can be attached to them. The knee jerks may be absent in the acute stage ; the plantar reflex in some cases may show an extensor response. The abdominal reflexes are variable.

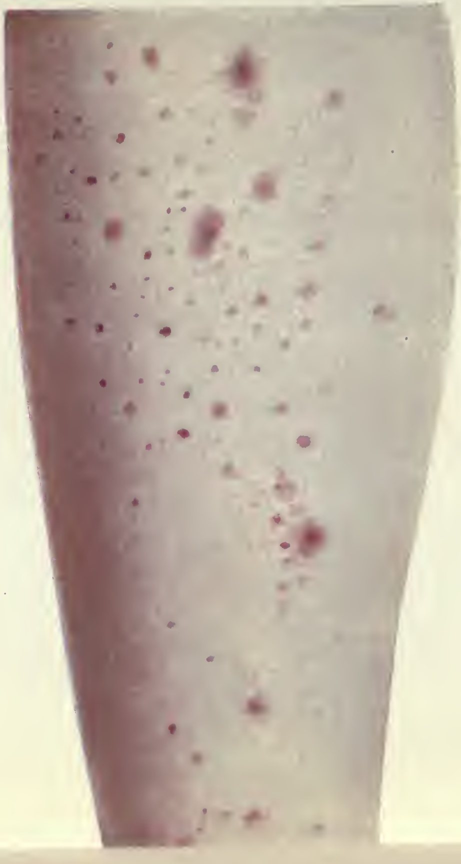
Paresis of ocular muscles may be observed though less frequently than in tubercular meningitis, the sixth nerve being usually affected. Nystagmus and diplopia occur in a small number of cases. Of other cranial nerves, the facial and hypoglossal are in some instances affected. The palsy is of a transitory nature and passes off with convalescence. Hemiplegia occurs but rarely, being observed in but 12 instances in 502 cases in the Royal Navy. Of the special senses, the eye and ear are affected. The pupils are usually dilated, and may be unequal. Conjunctivitis is fairly common, and iritis a rare complication. Panophthalmitis with consequent destruction of the eye-ball is rare. Optic neuritis is uncommon in comparison with its frequency in other septic forms of meningitis. Worster Drought and Kennedy found it five times in 80 cases; Cooke and Foster twice in 40 cases. Deafness is the commonest abiding defect left by the disease. It occurred six times in 120 cases observed. It appears within the first week and is usually permanent. Otitis media is an uncommon complication.

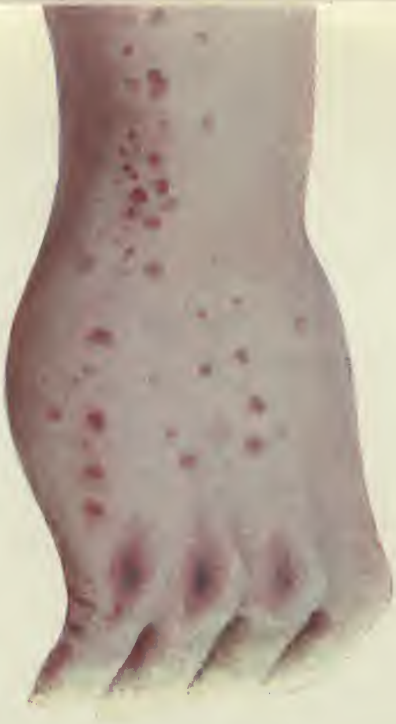
In acute cases rapid wasting occurs about the fourth or fifth day and continues while symptoms persist. In hydrocephalic cases the marasmus reaches an extreme degree. Arthropathies, in which the synovial membrane rather than the cartilage or bone is for the most part involved, occur in a small percentage of cases. Rolleston found them in 4·8 per cent. of 502 cases in the Royal Navy. Such arthropathies must be distinguished from those incidental to serum sickness; the joints are swollen and tender, and the meningococcus has been recovered from the effusion. The effusion is usually of short duration and rarely requires aspiration. Subsequent pain or stiffness is an uncommon event.

Reference has already been made to the fact that naso-pharyngeal catarrh is in no sense an essential feature of the disease. Bronchitis is a complication in a certain proportion of cases and may be of the fetid type. Broncho-pneumonia, usually of pneumo-coccal origin, is a relatively common complication, especially in comatose cases. In some instances the meningococcus is the exciting cause. Lobar pneumonia is an uncommon complication. Pleurisy may occur, and in hæmorrhagic cases, hæmothorax. In acute fatal cases, undulant breathing of the cerebral type or Biot's breathing is a notable feature, and Cheyne-Stokes' breathing may be a terminal phenomenon.

Slowness of the pulse in relation to the temperature is one of the most marked of the circulatory symptoms and may be regarded as due to vagus inhibition. In fulminating or acute

Plate II.





CEREBRO-SPINAL FEVER—MACULAR RASH.

cases the pulse is rapid and feeble from the first. Pericarditis is an occasional complication and the meningococcus has been recovered from the lymph. Endocarditis is rare. It is remarkable what little impress a disease of such severity leaves on the circulatory system during convalesence.

The alimentary canal suffers but slightly beyond the initial vomiting, which in some instances may be accompanied or replaced by diarrhœa, or even by mucous diarrhœa. Acute abdominal pain at the onset may tend to obscure the diagnosis.

The blood shows a polymorphonuclear leucocytosis usually about 25,000 per c.mm., rarely as high as 50,000.

Urinary changes are of slight importance. Hæmaturia may occur at the onset, even in cases without a hæmorrhagic rash. Febrile albuminuria is not uncommon while glycosuria is a rare complication. True nephritis is rare. Owing to the frequency of retention or overflow incontinence, cystitis and pyelitis are not uncommon. Further experience has not confirmed Sophian's view of their meningococcal origin. As in all febrile affections, epididymitis and orchitis occasionally occur, and the meningococcus can be recovered by puncturing the affected organ.

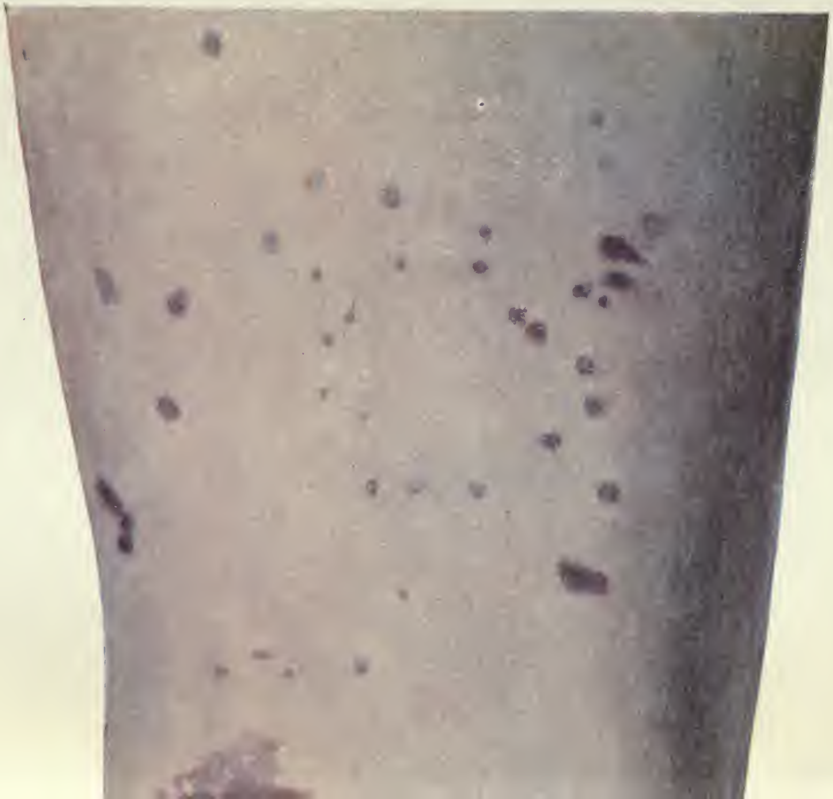
A study of a large number of cases reveals the fact that clinically the course of the disease runs in a variety of well-marked types. Primarily these may be differentiated into acute, in which either death occurs or the patient is on the way to convalesence in a fortnight, or chronic, in which the issue is doubtful for a longer period. Acute cases may be divided into fulminating cases, acute fatal cases, acute cases which recover, and abortive cases.

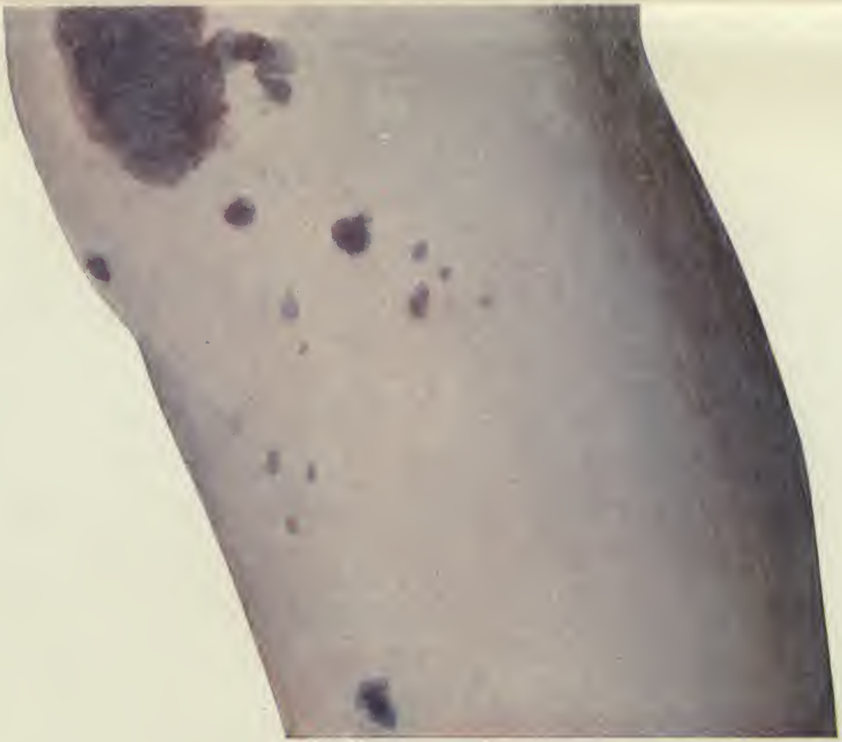
Fulminating cases may be defined as those in which death occurs within 24 to 36 hours after onset. These cases fall into two categories ; of these the first is constituted by those comparatively rare instances in which death is due to meningococcal septicæmia, the meninges showing no pathological change, purpuric spots and the presence of the organism in the blood affording the only means of diagnosis. The second and far commoner form presents even at that early stage well marked purulent meningitis. The onset is of startling suddenness ; a man may fall down unconscious on parade or be seized with epileptiform convulsions or maniacal excitement. More commonly, however, he goes to bed in his usual health, and is found unconscious or even dead in the morning. Vomiting may occur before consciousness is lost. Within the first few hours, large purpuric spots, which may contain meningococci, make their appearance on the trunk, extremities and face. The temperature is usually but slightly raised or even sub-normal though hyperpyrexia may occur. The face is pale or cyanosed, the hands tremulous and bathed in sweat, the pulse rapid and feeble, often uncountable. The breathing is often undulant and dyspnœa a marked symptom, the patient beating the air in his struggles for breath. Kernig's sign is often absent and head retraction rarely has time to develop. The cerebro-spinal fluid usually contains an increase of polymorphonuclear cells. Meningococci may or may not be present, but can usually be recovered from the cerebral ventricles post mortem. Fulminating cases are comparatively infrequent; two cases only occurred in 120 consecutive cases under the care of Colonel Foster. Such cases are stated to occur more frequently in the earlier months of an epidemic, and this general impression is probably, in the main, correct.

The acute fatal type may be defined as one in which death occurs within the first week from onset, usually within the first five days. Rolleston's figures show that of 86 deaths occurring in 225 naval cases in the third and fourth years of the war, 40 to 44 per cent. occurred on or before the fifth day. It must further be remembered that these results were obtained when early diagnosis and prompt treatment had been brought to a high pitch. The striking clinical feature in these cases is that their course is uniformly downward, as though protective reactions were totally unable to develop. The onset is sudden and headache severe from the first. Vomiting comes on early, and is soon succeeded by delirium. A petechial rash makes its appearance on the first or second day, retention of urine about the same time. Head retraction develops at an early stage. The pulse is usually rapid, the breathing shallow and undulant, the face and extremities early become cyanotic. Delirium may be violent, is usually attended by extreme restlessness, and quickly lapses into coma. The cerebro-spinal fluid is usually obviously purulent, and contains in the smear large numbers of extra-cellular meningococci which grow readily on cultivation.

The acute cases which recover present the symptoms described above though in a lesser degree. The onset is sudden, and headache severe ; vomiting occurs, usually during the first day. The second day may show not only no aggravation, but even an elusive improvement. With the onset of the third day, all the symptoms become accentuated, the delirium is often violent, and in many cases is succeeded by coma, retention of urine and inability to swallow. Dyspnoea, cyanosis and cerebral breathing, on the other hand, are not such marked features as in

Plate III.





CEREBRO-SPINAL FEVER—PURPURIC RASH.

the fatal cases. On the fourth day herpes may occur about the lips and a macular rash on the abdomen and extremities. The fundamental difference between the fatal acute cases and the acute cases which recover is that, in the latter, treatment begins at once to produce some improvement. During the fourth and fifth days there may be but little change except that the patient does not become obviously worse. From the fifth to seventh day improvement sometimes of the most dramatic character takes place. Once begun this usually continues with considerable rapidity, consciousness returns, and with it natural sleep ; the bladder resumes its functions, and head retraction disappears. Following this amelioration of symptoms, there may be fresh outbursts of fever accompanied by headache, vomiting and rigidity of the neck, due to the lighting up of fresh foci of infection, these recrudescences yielding in their turn to fresh administration of serum.

During every epidemic, but notably towards its close, cases occur which are characterized by headache, vomiting, some rigidity as manifested by Kernig's sign, or slight stiffness of the neck. The cerebro-spinal fluid shows an increase of polymorphonuclear leucocytes, and generally meningococci may be grown. In other instances, the fluid is sterile but the organism can be cultivated from the throat. In these cases recovery takes place in a few days. They are consequently described as abortive cases.

The chronic types of the disease may be divided into suppurative, hydrocephalic, relapsing and recrudescent.

In the suppurative type of case, as the disease progresses, the fluid obtained from the theca becomes increasingly thick and coagulated, until finally lumbar puncture yields only a few drops. This increasing density of the pus begins about the fourth or fifth day and continues in an augmented degree until death, which usually occurs in the third week. The patient wastes rapidly, the sphincters become affected, but instead of coma or violent delirium, the patient passes into a state of hebetude varied by periods of complete consciousness. This type of the disease is rare ; it occurred twice in Gaskell and Foster's 120 cases, is always fatal and neither the injection of serum nor washing out the theca with salines or citrate solution has any effect upon the density of the pus. The aberrant character of the exudation does not appear to depend on any specific difference in the infecting organism. Worster Drought and Kennedy found equal numbers of Types I and II infections.

In discussing the acute fatal type of cases, it was shown that nearly half the mortality of the disease occurred within the first week. With the exception of death due to intercurrent cause, practically the other 50 per cent. of deaths are due to hydrocephalus. Pathologically, hydrocephalus arises from adhesions forming in the arachnoid membrane, which interfere with the circulation of the cerebro-spinal fluid, giving rise to a loculated meningitis, and, as a corollary, distension of all the spaces of the cerebro-spinal system above the obstruction. The latter is in the majority of cases due to matting together of the areolar tissue in the roof of the fourth ventricle, but sometimes to adhesions between the parietal and visceral arachnoid in the cord.

It appears probable that adhesions form comparatively early and only begin to give rise to symptoms at a later date. In the acute fatal cases, adhesions are not as a rule observed, but in a case dying from intercurrent causes on the tenth day, the third and lateral ventricles were dilated. Again in a case trephined on the eighth day from onset, the roof of the fourth ventricle was densely adherent. A gush of fluid escaped from which the meningococcus was grown, while only 16 c.c. of sterile fluid had been obtained by lumbar puncture. This case is of interest as showing that complete occlusion may arise as early as the eighth day and further that about 16 c.c. may be taken to be the measure of the contents of the theca below the foramen of Magendie. However early the obstruction may be formed, the train of symptoms to which it gives rise does not develop until the second week. The acute symptoms have by then subsided, but agonizing headache continues. This is temporarily relieved by lumbar puncture. Towards the latter part of the second week more distinctive symptoms arise. The patient rapidly sinks into an adynamic state, with profuse sweating, incontinence of urine and fæces and a feeble pulse. Low muttering delirium, with a temperature of 100° to 101° and vomiting are present. Head retraction becomes more marked, and other forms of rigidity make their appearance, the legs and arms become flexed, and hyperæsthesia causes any movement to be attended by intense pain. Very rapid wasting takes place, and the patient passes into a semi-imbecile state in which he dies. Lumbar puncture yields a daily diminishing amount of progressively clearer fluid which is usually sterile, until only 10 to 15 c.c. are obtainable. In other cases the onset is more insidious. Usually the advent of these symptoms heralds a fatal result, but in a certain number the symptoms gradually pass off, the amount of cerebro-spinal fluid yielded by lumbar puncture increases day by day and complete convalescence results. It can only be conjectured that collateral sources of circulation are opened up until equilibrium is established. From the study of morbid anatomy and clinical symptoms presented by hydrocephalus the practical point may be deduced, namely, that the anatomical disposition of the areolar tissue at the roof of the fourth ventricle renders this site peculiarly liable to adhesive inflammation and consequent blocking of the channels of circulation. As a rule of practice, therefore, every effort must be made to overcome the source of infection at the earliest date possible by the administration of serum ; and further when this has been accomplished, repeated lumbar puncture must be practised to ensure that there is no stagnation in the circulation of the cerebro-spinal fluid.

In dealing with recrudescent or relapsing cases, the difficulty lies in the definition of what constitutes a true relapse. Recrudescences of fever and symptoms are common enough ; further, as Sophian has pointed out, a slight and unsuspected degree of hydrocephalus may produce an apparent relapse after a considerable interval of convalescence. Netter regards a true relapse as distinguished from a recrudescence by its occurring at least one month after all symptoms have disappeared. Even under these circumstances a relapse is presumably due to activity in a quiescent focus, since a second attack of cerebro-spinal fever is a very rare event.

Recrudescences after apyrexial periods of five to ten days are far from uncommon, and may be regarded as due to activity of a focus in the choroid plexus, hitherto untouched by serum, or possibly fresh infection from the naso-pharynx. Clinically recrudescences are marked by a sudden rise in temperature, with headache and often vomiting ; on puncture, the meningococcus can usually be grown. The attack usually yields rapidly to serum treatment. Recrudescences may repeat themselves for a variable number of times ; up to six have been observed. The course of cerebro-spinal fever is a lengthy one. Although acute symptoms may have entirely subsided within ten days, the necessity for watchfulness as regards recrudescence, or the possible supervention of hydrocephalus, involves confinement to bed for a considerable period. Kernig's sign is the last symptom to disappear, and until this has been consistently absent for five days the danger of a recrudescence or latent hydrocephalus is not past. Convalescence is somewhat slow, as occasional headaches and pain in the back may interfere with exercise.

Of the sequelæ, those connected with the eye and ear are by far the most frequent and permanent. Deafness usually appears by the end of the second week ; in a few cases it passes off with convalescence, but as a rule the loss of hearing is complete and permanent. The labyrinth is the part affected, and the affection is generally bi-lateral though occasionally only one side is affected. Though the commonest form of abiding disability, the incidence of deafness is not large. Rolleston found it 26 times in 502 naval cases or 5 per cent., Foster in six out of 120 cases. Panophthalmitis with consequent destruction of the eye-ball and optic atrophy are the only permanent lesions affecting the eye. The number of cases of the former is small; Rolleston gives 1·4 per cent. In 200 cases observed by Foster this complication occurred once. The affection is usually uni-lateral; though both eyes may be affected, the right eye is more frequently affected than the left. Blindness from optic atrophy is extremely rare among adults, in contrast with its comparatively frequent occurrence in posterior basic meningitis of infants. Hemiplegia is an uncommon sequela, cases presenting this complication being frequently fatal. In most instances the lesion is organic, and to some extent permanent. Some cases present a staggering gait with exaggerated reflexes, volitional tremors and nystagmus. Recovery here again, though slow, is usually complete.

Monoplegias with pain, wasting and loss of electrical reaction, as described by Netter, Horder and others, completely recover. Pain and stiffness of the back is a common complaint amongst convalescents. It has been attributed to repeated lumbar punctures, but may be observed in cases which have only received one puncture. Though perfectly well in other respects, these men are unable to bear their packs for some time, and this has been observed in soldiers who were candidates for commissions, when a motive for malingering was presumably absent. This disability entirely disappears in the course of two or three months. Headache is a residual symptom met with in a number of cases. It is recurrent often at considerable intervals, is relieved and often permanently cured by lumbar puncture, and is rarely permanent. Epilepsy, dating from an attack of cerebro-spinal fever, has been recorded. Mental changes of a permanent character practically do not exist; as with all acute and painful diseases, a certain proportion of convalescents show symptoms of neurasthenia, marked by concentration upon their own symptoms and feelings. With outdoor life and exercise these symptoms entirely disappear. With regard to symptoms other than those associated with the central nervous system, it is remarkable how slight an impress a disease of such severity leaves upon the body at large. The heart muscle is entirely unaffected. Convalescents from this disease contrast markedly in this respect with those recovering from the enteric group. The kidneys are entirely unaffected; anæmia, dyspepsia and disordered action of the bowels are of uncommon occurrence.

Prognosis.

With regard to prognosis, the signs and symptoms of the patient, his age, and the effect of treatment and the date at which it is begun, must be taken into consideration in each individual case.

As regards individual signs, onset characterized by sudden lapse into coma is of grave significance, although a few cases recover. A purpuric rash appearing in the first 24 hours is a grave symptom. A petechial rash appearing on the first or second day is an unfavourable sign. Cyanosis, extreme dyspnœa, cerebral breathing, and a feeble-running pulse are of fatal augury. Extreme restlessness is a more unfavourable sign than either delirium or profound coma. The temperature forms no criterion of the probable course of the disease, except that a low temperature with an apoplectic form of onset is an unfavourable sign. In the later stages hydrocephalus is a grave complication, few cases recovering. Recrudescences, however numerous, are not dangerous except in so far as each burst of infection brings with it the danger of resulting hydrocephalus.

As regards the age of the patient, the mortality rate is lowest according to Netter, at the fifteenth year; it then rises slightly till the twentieth year. After full maturity is reached it falls during the decade 20 to 30. After 30 it rises abruptly, and continues to rise with each decade of life. In a patient over 30 the outlook is always grave.

As regards the effect of treatment, the most important point is the day on which treatment is begun. Flexner's early statistics demonstrated a marked difference in the results obtained when efficient serum treatment was begun at once, or when an interval of two or three days elapsed. Martin Flack's results in the London district bring out this point very clearly.

The remote prognosis of cerebro-spinal fever has already been touched upon in treating of the sequelæ of the disease. In dealing with troops, two administrative problems arise—the length of hospital and convalescent treatment with the resulting period of invaliding, and the amount of permanent disability, which may give rise to a claim to pension.

In dealing with the first of these questions the nature of the disease involves, in the majority of instances a prolonged stay in hospital. This may be further extended by the necessity for swabbing until the naso-pharynx is free. Thus a case which yields rapidly to treatment is rarely fit for convalescent treatment under a period of 20 to 30 days. When recrudescences occur the period may extend to 50 or 60 days. Once convalescence is established the subsequent progress is rapid, so that many cases who are prolonged carriers are fit for duty by the time the naso-pharynx is free.

The question next arises as to the incidence of a disability of such a nature as to give rise to a claim for pension. Two sources of information have been utilized—the records of the Hitchin Convalescent Home and the records of the Ministry of Pensions. The Hitchin Convalescent Home was opened on May 5th, 1915, as a provision for all cases of tardy convalescence arising in military hospitals in the United Kingdom. This would also include cases of the same character evacuated from hospitals overseas. During the years 1915–16, 93 cases were admitted ; of these 89 returned to duty, two were invalided out, and two transferred to other hospitals. During the years 1917–18, 254 cases were admitted. Of these 126 returned to duty, 25 were disposed of as chronic carriers, and the remainder transferred to other hospitals. Thus even in chronic cases two-thirds of the patients are fit for duty.

A further source of information is in the records of the Ministry of Pensions. Dr. H. W. Kaye has furnished reports of the Re-survey Boards, from 30th June to 1st November, 1919. During this period 254,374 men were examined and 22 cases claimed their invaliding disability as due to cerebro-spinal fever. It is probable that a certain number of other cases claimed disability on account of deafness, or the loss of an eye, or possibly rheumatism, and thus are not shown under this heading. In any case the fact remains that only this infinitesimal number of 22 men claimed disability on account of this disease. Of these 22 cases, the documents of 13 show that 11 were graded A., while two were graded B. on enlistment. Of the 11 A. cases at their latest re-survey the disability adjudged in 10 was as follows :—

10 per cent. and less than 20 per cent.	1
20 per cent.	4
30 per cent.	1
40 per cent.	3
70 per cent. (a case of complete deafness)	1

Of the B. cases one partially deaf on enlistment was adjudged 30 per cent. A second had been invalided out in 1901. At his last re-survey he presented tremor and wasting of left thigh and was adjudged 40 per cent. disability. The complaints of the men were, in the main, of pain and stiffness in the back, sometimes accompanied by tenderness on pressure, in others vertigo with recurrent headache, and in a few instances tremors. Of these complaints pain and stiffness in the back is a common symptom, the duration of which varies markedly in different cases. In reporting on the condition of the convalescents at the Hitchin Home this condition was one of the commonest, and varied markedly in the time in which it disappeared, but in no case did it form a permanent disability. In estimating the disabling effects of this disease, it must be remembered that while certain organic lesions, as above described, occur in a small proportion of cases, a large proportion present functional nervous troubles, which under appropriate conditions, the avoidance of hospitalism being the most essential, entirely recover. Further, except where these organic lesions have occurred, the man's ultimate efficiency is in no wise lowered by an attack of the disease. Two of the first 30 cases seen in 1915 early obtained commissions, a third, who ran a febrile course of 50 days with no treatment other than a diagnostic lumbar puncture, was, on the testimony of his platoon commander, one of the best soldiers in the battalion.

Diagnosis.

In diagnosing a case of cerebro-spinal fever it must be clearly understood that the only reliable diagnosis in fulminating cases is derived from the bacteriological examination of the cerebro-spinal fluid or of the blood. Lumbar puncture should be performed at once in all cases in which a doubt exists. By using the fine needles made by Gentile of Paris a diagnostic puncture can be made almost painlessly. In acute cases and when serum is given, an anæsthetic should be used. Dickson and Halliburton experimentally, and Flack clinically, have shown that anæsthesia markedly increases the flow of cerebro-spinal fluid, thus rendering the injection of serum in large quantities easier and safer. As a means of early diagnosis, and consequently efficient treatment, puncture must be performed before the clinical picture is in any sense complete. Both in England and France the tendency of medical officers was to wait for the appearance of distinctive symptoms, such as head retraction, before resorting to puncture, and thus to sacrifice valuable time. During the first 48 hours the symptoms may bear a general resemblance to those of any other acute infection ; the case may therefore remain undiagnosed because meningitis has not been thought of. It must be remembered that this disease is protean in its manifestations, the salient symptoms appearing more markedly in different systems in diverse cases, and varying notably in the time at which they become manifest. The points to which attention should be directed are the increasing severity of the headache, the possibility of eliciting Kernig's sign, and the most suspicious symptom of all, difficulty in micturition. The pressure at which the fluid flows is of slight diagnostic importance, and the appearance of the fluid itself unless obviously purulent is equivocal; a clear fluid may be heavily infected. In some instances the fluid at the first puncture shows a yellowish pigmentation with a tendency to clot. This is Froin's syndrome, and is of grave prognostic significance. A yellowish colour at subsequent punctures is common enough and only due to bleeding at the previous puncture.

The diseases from which a diagnosis has to be made are the acute specific fevers on the one hand, and other diseases of the central nervous system on the other. Of the acute specific fevers measles may cause difficulty, a macular rash being common to both, but the more severe headache and the presence of Kernig's sign distinguishes cerebro-spinal fever. Fevers of the enteric group differ in their gradual onset and in the absence of rigidity. Pneumonia in its early stages may be distinguished by the ratio of the pulse to the respiration, and the absence of Kernig's sign. In influenza Kernig's sign is absent and vomiting rare. Of diseases of the central nervous system, tubercular meningitis is the commonest cause of difficulty, but the slower onset, the more constant involvement of the cranial nerves, and the cell contents of the cerebro-spinal fluid, which in tubercular meningitis contains many lymphocytes and few polymorphonuclear cells, will settle the diagnosis. Meningitis due to infection by other organisms will be differentiated by the bacteriological examination of the fluid. In abscess of the brain the headache is more localized and optic neuritis more common. The cephalic form of acute poliomyelitis can be differentiated by the negative findings in the cerebro-spinal fluid. Encephalitis lethargica can be recognized in the same way. In the course of many febrile affections a mimicry of meningeal symptoms occurs known as meningism. This condition can at once be recognized by the nature of the cerebro-spinal fluid.

Treatment.

With regard to treatment previous to the epidemic which occurred during the war, the researches of Flexner and Dopter had proved the efficacy of intrathecal injections of anti-meningococcal serum. On the outbreak of the disease amongst troops in 1914, serum treatment, however, yielded singularly disappointing results. Amongst the Canadians, there were 40 cases with 26 deaths, a mortality of 65 per cent., while Rolleston stated that in the navy the mortality for serum-treated cases was 60 per cent. Further researches were undertaken, which eventually showed that the requisites for an efficient serum were that it should correspond in type with the infecting organism and that it should be standardized and of proved anti-endotoxic power. A serum known as the M.R.C. was finally evolved, which yielded remarkable results. The serum is more efficacious against Type I than against Type II. Gordon's final results with the M.R.C. serum in military cases were :—

Cases.	*Deaths.*	*Percentage Mortality.*
249	79	31·72

Of these cases 141 were treated with serum before the seventh day, of which 27 were fatal, a mortality of 19·14 per cent.

The technique of serum treatment is simple. Lumbar puncture should be performed, and as much fluid run off as possible. A quantity of serum less than that of the fluid evacuated should be injected by the gravity method. The initial dose should be 30 c.c., and in severe cases 60 c.c. ; if under an anæsthetic, these quantities can usually be injected without danger. For the first dose pooled serum of Types I and II should be employed until the type of infecting coccus can be ascertained. A practical point is that the naso-pharynx should be swabbed, growth from this source being more rapid than from cerebro-spinal fluid. Identification of type is thus hastened. When the type has been identified, the appropriate mono-type serum, if available, should be administered. After injection, the foot of the bed should be raised to encourage the flow of fluid towards the base of the brain. Injections of 30 to 60 c.c. of serum should be repeated daily, according to the condition of the patient and the state of the cerebro-spinal fluid. Recrudescences should be treated by renewed serum treatment. It is of great importance that any recrudescence should be promptly recognized and dealt with. However slight the outburst, it always involves the possibility of subsequent hydrocephalus. Should more than ten days have elapsed since the last injection, the patient should be desensitized, either by the hypodermic injection of 1 c.c. four hours before treatment, or by Besredka's intravenous method. Should no serum be available, the drainage of the theca should be maintained by daily lumbar puncture, a method of treatment which yielded good results before efficient sera were available. When the pus is very thick, the theca should be washed out with normal saline or citrate solution. A considerable proportion of cases develop a serum rash often accompanied by arthritic symptoms, manifestations seldom dangerous and alleviated by pituitrin. Herrick claims good results from intravenous injection of serum in early cases yielding positive blood cultures. Large doses, 200 to 400 c.c. in all, are given. Since the procedure is not without danger from anaphylactic shock, each patient should be tested for hyper-sensitiveness by an intracutaneous injection of 1/10th c.c. of serum, which in sensitive cases produces a local reaction, characterized by redness, œdema and swelling, within 40 minutes. Netter and Sainton advocate the obviously safer course of intra-muscular injection. In any case, it must be remembered that the essential danger to life lies not so much in the blood condition as in the suppurative processes in the brain and cord, so that intrathecal medication must form the basis of all sound treatment.

Injections either intra-muscular or intravenous of soamin or hexamine have yielded results far inferior to serum treatment. Vaccines have been employed, but without sufficient success to lead to their general adoption. In hydrocephalic cases, surgical measures have been attempted. These consist either in draining the lateral ventricle after trephining, or trephining from the posterior fossa, raising the cerebellum and draining the fourth ventricle. These procedures have met with but slight success, but as the condition is otherwise hopeless, they give a chance of recovery.

As regards general treatment, headache and restlessness are best controlled by morphia, which may be freely given. The diet should be nourishing, alcohol given in the acute stages, but withheld later. Maclagan and Cooke recommend the intra-muscular injections of liq. adrenalin in 10 mm. doses four-hourly in adynamic cases. In comatose cases the throat should be constantly swabbed out.

On reviewing the results of the epidemic during the past five years, one fact stands out with startling clearness, that whereas the mortality among civilians remained substantially the same, the military death rate showed a marked and progressive decline. The curves in Chart I demonstrate this fact.

It may be argued that the higher civilian death rate is due to the greater mortality among infants, but the analysis made of the fatality of those from 20 to 30 years of age, and therefore physically comparable to the average soldier, negatives this view. The explanation is probably to be sought in the fact that military cases were all segregated into hospital centres, adequately equipped bacteriologically. Consequently no time was lost before efficient serum treatment was begun.

Early in 1915 one or more centres were formed in each command to which all suspected cases were sent for diagnostic lumbar puncture and bacteriological examination. These centres were formed for the most part in military hospitals and territorial force general hospitals. A skilled bacteriologist was appointed to the laboratory in each centre, while an adequate supply of serum was always available. Orders were issued that no diagnostic lumbar puncture on a suspected case should be performed outside these centres. Apart from better facilities for treatment the extremely low vitality of the meningococcus rendered any attempts at culture other than those on the spot practically valueless. Further, the differentiation of the type of infecting organisms in order that the serum employed should be of like type, necessitated a special technique which was only available in such centres. Experience gained during the war

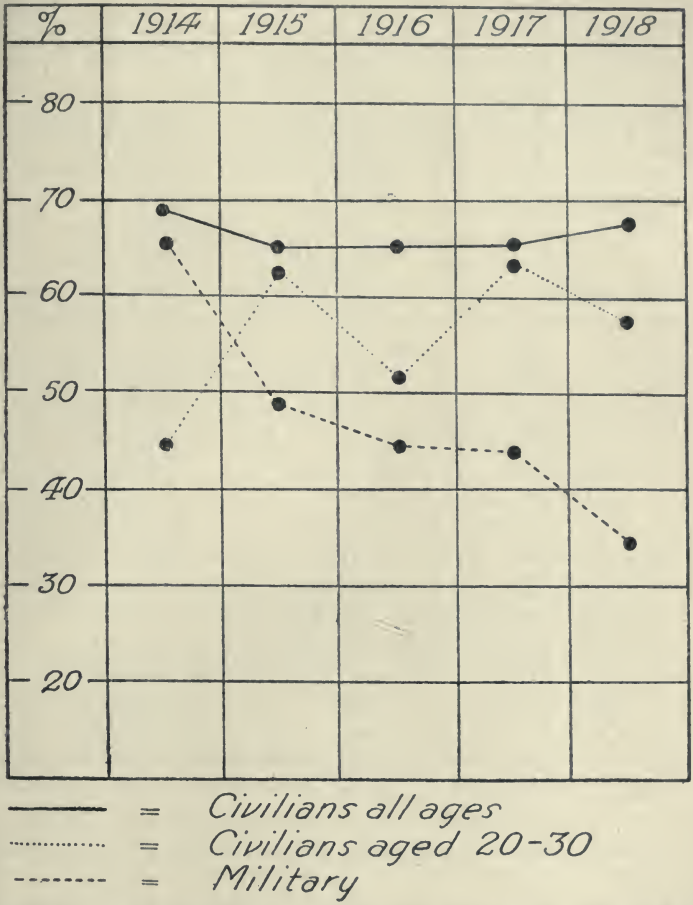


Chart I.—Showing fatality of cerebro-spinal fever in the civil population of England and Wales, and amongst troops in training in the United Kingdom respectively for 1914–1918.

has shown that even the gravest cases can be transported long distances by car or rail without any serious detriment. Moreover, the slight risk incurred in transport is infinitely less than that of foregoing efficient treatment from hesitation to move the patient. In France similar administrative measures were adopted, centres being formed in advanced areas as well as at the base, to which all suspected cases were sent. In these elaborate precautions may well be the cause of the difference between the civil and the military statistics.

As regards the treatment of carriers, it may be stated that although sprays, notably chloramine T., have temporarily reduced the carrier rate, the most certain method of freeing the throat from infection is abundance of fresh air.

Prevention.

With regard to preventive measures, experience gained during the war has led to the accumulation of a mass of observations whence generalizations as to the spread of the disease could be formed. Military administration, moreover, enabled preventive measures to be rapidly put in force and efficiently carried out. The researches of Flack, Glover and others showed conclusively that the carrier rate of agglutinable meningococci bore a direct relation to season, the rate falling through the summer months and rising during the winter. Glover's observations in the London District demonstrated the direct influence of overcrowding in increasing the carrier rate. Further, Glover proved that a decrease in overcrowding invariably led to a marked fall in the carrier rate. The corollary is that, as cerebro-spinal fever is largely caused by overcrowding, the first essential preventive measure is the strict observance of the hygienic rules already laid down. The provision of adequate lateral space in sleeping quarters is of primary importance, since the transference of infection by droplets from the upper respiratory passages is more likely to take place during sleep, owing not only to longer period of exposure but also to greater propinquity. In the event of the disease becoming prevalent in a unit in the field, it is advisable to bivouac these men out in fields, rather than to crowd them into out-buildings and billets. Chart II., drawn by Glover, immediately demonstrates the nature of the precautions to be observed.*

With regard to carriers, the development of cerebro-spinal fever in a carrier is a very rare event. Flack and others have recorded cases. But carriers transmit the disease to others by droplets from the upper respiratory passages. In this regard may be quoted Fildes' observations on the development of cerebro-spinal fever in a number of new recruits in the navy, in whom swabs from the naso-pharynx had proved negative on enlistment. Similar results have been recorded by other observers.

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* From Medical Research Committee's Report, No. 50, page 139.

The danger from carriers is particularly evident in the number of cases reported by Reece, Glover and others, in which a soldier carrying the meningococcus has infected his family while on leave. On the occurrence of a case the immediate contacts should be swabbed and carriers segregated from the others.

Where overcrowding is unavoidable, as during mobilization, and where there is reason to suspect a high proportion of carriers among a particular body of troops, an attempt should be made to reduce the spread of infection among these men by the general use of some mild disinfectant. Various methods are available for this purpose, such as gargling the throat and washing out the nose with a solution of 1 in 5,000 pot. permang. in normal saline, the solution being warmed before use.

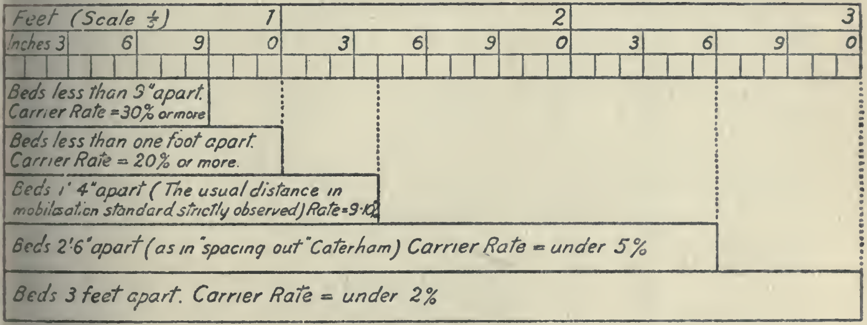

CHART II.—Relation of distance between edges of beds to carrier rate. Army plank beds 2½ feet wide in ordinary barrack-rooms and huts under war conditions.

But where large numbers of men have to be dealt with, a trial should be made of inhaling rooms, the air of which is charged with some finely divided disinfectant, the atomizer being worked by steam or compressed air. The men are treated in batches, according to available space, remaining in the chamber from five to ten minutes, during which time they inhale vigorously through the nose. This treatment should be carried on daily and has the advantage of not interfering with training. The disinfectants used in these chambers are either chloramine T. or sulphate of zinc. Of these chloramine T. was first used, but although the most active disinfectant in practice it was not well borne. In the later stages of the war zinc sulphate was used with satisfactory results. The strength of solution used was 2 per cent. in normal saline. Two forms of apparatus can be employed for this purpose :—

(*a*) A small portable spray, operated by steam generated by burning methylated spirit, called a Levick spray. Two instruments are necessary, one in operation while the other is being filled. One Levick spray charges the atmosphere of 1,000 cubic feet air space, which suffices for the treatment of 20 men at a time.

(*b*) For larger inhaling rooms a special jet devised by Lieut.-Colonel T. G. M. Hine was found to give satisfactory results. This jet is operated by steam under pressure generated from a boiler outside, or compressed air when available may be employed.

In employing these mechanical methods, it must always be borne in mind that abundance of fresh air is the most rapid method of freeing the throats of carriers from infection.

It must be remembered also that every patient who has the disease is a carrier, and the mental hebetude or delirium which so frequently marks the disease increases the danger of infection from naso-pharyngeal discharges. Therefore all such patients should be strictly isolated and early diagnosis is of the first importance.

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CHAPTER VII.

INFLUENZA.

ORDINARY influenza was never absent from the various army commands in the United Kingdom during the war. In 1916 there had been 36,072 admissions and in 1917, 28,980 admissions, the incidence in those years tending to be rather higher in the winter than in the summer. In 1918 the figures were about normal, until in June there was suddenly a great increase, as shown in the following table :—

Month.	Admissions.	Month.	Admissions.
January, 1918 ..	3,158	January, 1919 ..	4,547
February ,, ..	2,356	February ,, ..	13,752
March ,, ..	3,483	March ,, ..	7,709
April ,, ..	2,306	April ,, ..	2,954
May ,, ..	4,737	May ,, ..	1,017
June ,, ..	31,138	June ,, ..	416
July ,, ..	25,480	July ,, ..	381
August ,, ..	3,358	August ,, ..	281
September ,, ..	2,738	September ,, ..	365
October ,, ..	30,097		
November ,, ..	23,021		
December ,, ..	6,910		

In France the disease began by a few local outbreaks in the First and Second Armies in April and May 1918. It appeared both in Rouen and Wimereux in April. At the end of May it reappeared with great violence in the Second Army, spread apparently a little later in the First and Third, and in the Fourth Army from about the end of June.

The numbers affected were very great. The Second Army admitted to its casualty clearing stations 1,921 cases during the week ending 12th June, and 3,851 cases during the week ending 19th June. From 25th June the rate fell rapidly and by the middle of August it had sunk to 50 daily. The First Army admitted 36,473 cases to its casualty clearing stations between 18th May and 2nd July. The Fourth Army admitted to casualty clearing stations during the week ending 1st July 2,705 cases, and 3,480 cases during the week ending 8th July.

This epidemic died down in August, though perhaps it did not wholly disappear. At the end of September the disease began to spread again.

On 5th October 1918, the disease was made notifiable in the British Armies in France, and the numbers for the succeeding weeks during 1918–19 were as follows :—

Week ending	Admissions.	Deaths.	Week ending	Admissions.	Deaths.
Oct. 12th	1,776	—	Dec. 28th	2,579	73
Oct. 19th	3,080	2	Jan. 4th	2,768	34
Oct. 26th	9,280	314	Jan. 11th	2,195	32
Nov. 2nd	13,203	701	Jan. 18th	1,888	33
Nov. 9th	11,877	878	Jan. 25th	1,563	40
Nov. 16th	7,389	689	Feb. 1st	2,354	69
Nov. 23rd	8,008	546	Feb. 8th	3,074	104
Nov. 30th	8,206	526	Feb. 15th	4,011	144
Dec. 7th	7,087	412	Feb. 22nd	5,768	212
Dec. 14th	6,033	213	Mar. 1st	3,502	200
Dec. 21st	3,919	121	Mar. 8th	2,714	140

The acme of incidence was in the week ending 2nd November, 1918 ; the acme of mortality was, as might be expected, a week later. But a curious difference is found at the end of January, when the mortality began to rise before the incidence. The fatality cannot be calculated weekly, as the cases dying in any given week are largely composed of cases admitted before that week began. On the total it is almost 5 per cent. of the cases admitted, 112,274 admissions to 5,483 deaths.

The same curve with three waves, in June and November 1918, and February 1919, was reproduced in the figures for the civil populations of Copenhagen and London, and for the troops in the United Kingdom.

The disease was world-wide, and its course seemed to be from west to east. It prevailed in America in 1917. In 1918 the first European epidemic on a large scale took place in Spain in May. It invaded France, Italy and Germany, and weakened the effective strength not only of the Allied but of the German Armies as well. It was rife in Macedonia and Egypt. It caused great mortality in India, and in the late summer was very severe in South Africa, where monkeys and baboons are said to have died of it.

In Mesopotamia, 100 cases of a three-day fever were reported at the end of June in a batch of men returning from leave in India. The fever so closely resembled sand-fly fever, which was prevalent, that for several weeks medical officers could not be persuaded that the new disease was anything else. By the middle of July it had spread up to the front and was evidently very contagious. On 6th August, orders were issued to return the new epidemic as influenza. No accurate figures are available for July, but in August and September 1918 there were admitted to hospital a total of 8,026 cases, of whom 3,337 were British and 4,689 Indians. These figures, however, give little idea of the extent of the epidemic, as the majority of cases were treated in unit lines. It caused a great increase in the admission rate and it swelled the death rate, though it had little or no effect in increasing wastage by invaliding. In October its severity was increasing, and it reached its acme in the second week of October. During the last quarter of the year there were 16,961 admissions to hospitals, equal to 41 per 1,000 of strength, the British showing a higher admission rate, 79 per 1,000, than the Indians, 28 per 1,000, but the Indian admission rate and case mortality for pneumonia were much higher than the British. The mortality for influenza, allowing for many deaths recorded as pneumonia, was reckoned at 6·5 per cent. of cases in this quarter of the year. Thereafter the numbers fell gradually until in April 1919 they became negligible. There was no such recrudescence of the epidemic in the first quarter of 1919 as occurred in England and France.

It was noted in England, Germany and elsewhere that mortality was specially great between the ages of 25 and 40.

The disease was extremely infectious. In an army school, 320 strong, 90 men, and in a labour company 520 strong, 140 men, were found ill at one visit. A brigade of artillery lost a third of its strength in 48 hours, and in a brigade ammunition column on one day only 15 out of 145 men were fit for duty.

Symptoms amongst Troops in the United Kingdom.

The epidemic in England may be subdivided into two parts, both acute and widespread, but quite distinct in clinical type and mortality, namely :—

(1) The acute and very widespread "three-day fever" epidemic of June–July, 1918, with very few fatalities.

(2) The severe "pneumonic" type of the winter of 1918–1919, with a considerable mortality from pulmonary complications.

During the summer epidemic the first case of influenza would occur in the midst of perfect health in a circumscribed community, such as a barracks or a school, and within the next few hours or days a large proportion, occasionally even every single individual of that community, would be stricken with the same type of febrile illness. The patient would be seized rapidly, or almost suddenly, with a sense of such prostration as to be utterly unable to carry on ; he would be obliged to lie down where he was, or crawl with difficulty back to bed, so that barrack rooms which the day before had been full of bustle and life would now be converted wholesale into one great sick room. The hospitals were, within a day or two, so overfull that fresh admissions were impossible and the remainder of the sick had to be nursed and treated where they were.

The men's temperatures were raised to varying heights, generally about 103° or 104° F. ; the pulse rates were less raised in proportion ; the tongue was coated, the face flushed, and the eyelids a little drooped as though the patient were but half awake. There was often huskiness of the voice, the throat was sore, and there was some frothy expectoration from the pharynx and larynx. There was some reddening of the fauces and pharynx, and in some cases the tonsils, besides being reddened, looked swollen and enlarged, and there might be tenderness on either side of the upper part of the neck below and behind the angle of the jaw, suggesting that the lymphatic glands here were inflamed too, though palpable glandular enlargement was not as a rule found. Headache, made worse by a change of posture or by the effort of coughing, was prevalent.

Thus lassitude and general aching, with fever, a coated tongue, loss of appetite, soreness of the throat, huskiness of the voice, and headache were the main symptoms.

Most patients slept well and asked simply for water and cooling drinks. The temperature in many was already coming down to normal at the end of the second day, and in most it had become normal at the end of the third day, and remained so thereafter. The patient by this time was feeling almost himself again, asking for food, wishing to get up, and complaining of little more than some remains of soreness of the throat and perhaps some huskiness of voice. Convalescence was rapid and the great majority of the patients were fit for their ordinary work again by the end of the week.

There was practically no mortality.

There was no albuminuria ; no special tendency to infection of the accessory nasal sinuses ; indeed no tendency to any particular complication at all. Hundreds of cases ran very much the same course, and "three-day influenza" was the popular name generally given to the disease.

Contrasted with this extensive and acute but non-fatal outbreak of the summer of 1918, the world-wide "plague" of influenza of the following autumn and winter, with its millions of deaths, presented very different clinical characters. Those who had experienced the minor epidemics of "purulent bronchitis with heliotrope cyanosis and fatal ending" that had occurred here and there in military camps in America, England and France during 1916 and 1917, had already become familiar with some of the worst features, especially the dreaded blueness of what was probably the same malady under a different name; but now it was a question of seeing hundreds of cases in districts in which the fatal "purulent bronchitis" had affected but a few.

Nevertheless, it is important to emphasize the fact that these fatal "pneumonic" cases constituted but a minority of the whole. There were far more cases of ordinary typical benign influenza than there were of "influenzal pneumonia." Broadly speaking, out of 1,000 individuals stricken by the disease fully 800 had no more than an ordinary attack of uncomplicated "influenza," a little more severe perhaps than the "three-day fever" of June 1918, but not any worse than simple influenza as it may occur at any other time. In the remaining 200, "pneumonic" symptoms were added to those of simple influenza, and of these about 80 died. The most ominous symptom was the heliotrope cyanosis. It developed in less than half of the pulmonary cases, but once it became definite the prognosis was so bad that out of every 100 "blue" cases about 95 died.

Even the mildest case had to be regarded as potentially grave; no matter how benign the illness might appear to be at first, the pulmonary complications and cyanosis might set in without any notice at all. A patient might have been ill a day or two with mild influenza and seem to be progressing well; in an hour or two the whole picture might change, and twenty-four hours later the patient might be dead. During the epidemic itself, therefore, every case had to be regarded as in grave danger. It is only on looking back that the two great classes—800 out of every 1,000 mild and ordinary; 200 out of every 1,000 severe, pulmonary, grave—emerge clearly into view.

In these latter, although the pulmonary complications were spoken of as "pneumonia," the one thing they hardly ever showed was ordinary croupous lobar pneumonia in the recognized sense of the term. Although the occurrence of dullness, bronchial breathing, bronchophony, pectoriloquy and crackling râles over the greater part or whole of one lobe was frequent enough to make those who saw no autopsies believe that there was real lobar pneumonia present, yet it was only in exceptional cases that croupous lobar pneumonia was found post-mortem. The "pneumonia" was an acute infective pulmonary inflammation in which such consolidation as resulted was due, not to croupous lobar pneumonia of the classical sort, but to a conglomeration of changes which included bronchitis and peribronchitis, coagulative œdema, hæmorrhage, collapse, broncho-pneumonia, abscess formation and compression by pleuritic effusion, totally different from anything ordinarily seen in the post-mortem room. Hence, in speaking of these cases as "pneumonic," it must be emphasized that the pulmonary inflammations implied were those peculiar to the epidemic, and not just croupous lobar pneumonia complicating influenza.

The "pneumonic" complications would develop at any period of the influenzal attack. In most cases the patient had been ill for a day or two with ordinary simple influenza, not necessarily more severe than that of his neighbours, when there was a rapid or sudden change for the worse, and the picture changed to that of severe disease of the lungs. The effects of the pulmonary changes were often so fulminating that death might ensue in 24, 36 or 48 hours, in such a way as to suggest that it was due not to the lung lesions themselves but rather to a generalised and very virulent microbic toxæmia, or actual septicæmia.

On the other hand there was often no preliminary "influenzal" period at all, the patient being attacked from the start in such a way that ordinary lobar pneumonia of virulent or even ultra-virulent type would have been the most likely diagnosis, if the case had occurred singly and not in such an epidemic.

Again, the pulmonary complications were often later in their development, yet equally fatal. The patient might have had no symptoms other than those of ordinary influenza for nearly a week; his temperature might be falling steadily, or might have become normal, so that danger might be regarded as past, and yet the "pneumonic" complications might set in and carry off a man who seemed almost convalescent.

Less often, and yet not infrequently, the patient might be apparently quite convalescent from "influenza," ready to be discharged from hospital, and yet go down with "pneumonic" symptoms and die.

All types were seen in abundance—the initial, the early, the later, and the latest.

At whatever stage the pulmonary complications set in the patient generally began to complain of pain in some part of his chest. In practically every case there was also cough, not always severe, but sometimes in itself distressing, short, dry and hacking to begin with, looser and associated with frothy, blood-stained or purulent sputum within a few hours, or on the following day. Towards the end of a severe case coughing and expectoration would be entirely absent from sheer weakness of the sufferer and inability to cough at all. The rate of breathing became accelerated out of all proportion to the physical signs; in the worst cases the respiration rate would rise to 40, 50, or even 60 to the minute, and yet without any particular evidence of respiratory distress. Orthopnœa was exceptional, and although the patients were breathing so rapidly they seldom, if ever, complained of actual difficulty; it was rather a polypnœa or tachypnœa, than a true dyspnœa. The condition of the skin was not constant; it might be hot, dry, and pungent as in ordinary lobar pneumonia; quite as often the whole of the patient's body and limbs would be covered with profuse perspiration, the latter often resulting in sudamina and miliaria. A rigor might occur at the onset of the pulmonary complication, but more often there was nothing in the way of a definite rigor to attract notice, though the temperature, already raised, might rise higher.

The pulse rate, though raised, was seldom unduly rapid, and it was a remarkable feature of a great majority of the cases that the condition of the pulse remained good almost to the very last, failing only *in articulo mortis*.

The physical signs varied widely, and as a general rule were remarkable by their paucity. There might be a few scattered rhonchi over the front of the chest and over the upper part of the back, with a few râles lower down, or there might be little more than deficient vesicular murmur at one or other base. Again there might be a patch or two of consonating râles, or even definite bronchial breathing over a considerable area of a lower lobe, and yet later, on the same day, these signs might disappear entirely. Pleural friction, most often at the back or in the axilla, was heard in a large number of cases. The extent, however, of the physical signs bore little relation to the degree of illness of the patient, or to his cyanosis. A man might be of heliotrope colour with hardly any lung signs, or he might have signs of consolidation of both lower lobes and not be blue at all. Subcutaneous emphysema of the chest wall was occasionally seen, and was of bad omen. On the other hand, not a single case of spontaneous pneumothorax was observed.

Herpes facialis occurred, sometimes in a very severe form. Herpes of the pinnæ was several times seen. A localized purpuric eruption on the legs was sometimes found, and in two cases this was followed by hæmorrhagic bullæ with œdema, which subsequently ulcerated. Both these patients died. Erythematous areas were occasionally seen.

Epistaxis was strikingly common at the onset. Hæmoptysis was also common. Hæmatemesis was many times observed, sometimes no doubt from swallowed blood, but occasionally

Plate IV.

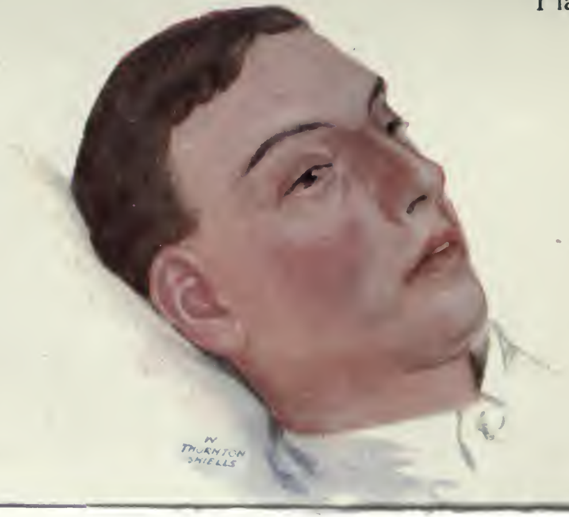


Fig. 1.—This illustrates an early case in which the facial colour is frankly red, and the patient might not appear ill were it not for the drooping of the upper eyelids, giving a half-closed appearance to the eyes.

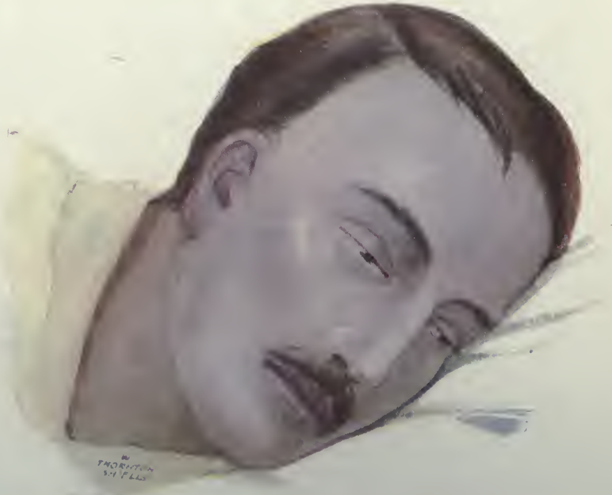
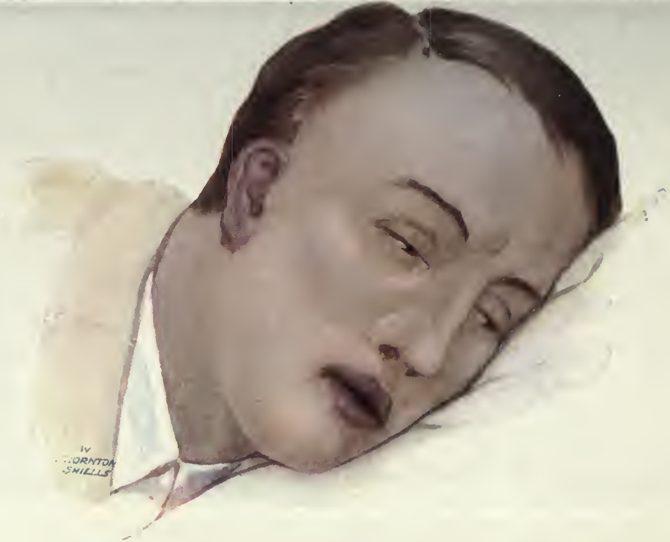


Fig. 2.—This illustrates a pronounced degree of the heliotrope cyanosis. The patient is not in physical distress, but the prognosis is almost hopeless.

Fig. 3.—This illustrates another type of the cyanosis, in which the colour of the lips and ears arrests attention in contrast to the relative pallor of the face. The patient may yet live for twelve hours or more.



THE "HELIOTROPE CYANOSIS" OF INFLUENZO-PNEUMONIC SEPTICÆMIA.

without doubt originating in the stomach itself. The prognosis was not necessarily bad.

The facies, at first flushed and red, with a peculiar drooping of the eyelids giving a weary look, shown in Plate IV, Fig. I, might remain purely red throughout, but in a large number of the cases affected by the pulmonary complications the red tint rapidly changed to one of progressive cyanosis, such as is depicted in the plates (Plate IV, Figs. 2 and 3). When this heliotrope cyanosis appeared the prognosis was altered so completely that a fatal ending was regarded as almost inevitable. A small percentage of cases recovered, even after the cyanosis had developed, but the great majority succumbed, and it was among cases of this type that the great mortality of the epidemic occurred. There were, of course, cases which died without the cyanosis being pronounced, but in going round a large ward one could, without examining the patients at all beyond looking at their countenances, pick out those who were going to die with almost uniform certainty by reason of their colour alone. The cyanotic tint might be definite in a patient who was complaining little, was taking his liquid nourishment well, intelligently interested in his surroundings, answering questions promptly and clearly, and in fact without any indication, except his colour, that by the next day or the day after he would almost certainly be dead.

The drawings reproduced in Plate IV were taken from rather extreme cases, and very often the degree of fatal heliotrope cyanosis fell a long way short of that depicted. Whatever the degree of cyanosis, however, it rendered the prognosis bad.

In some the cyanosis might be well marked before the patient had been ill twenty-four hours, and death occurred in some instances within this time. In others the duration might be forty-eight hours. In others again, the lividity came on more gradually and the patient might remain alive for three, four, or five days, or even for a week, breathing 50 or 60 to the minute, not unconscious, not subjectively distressed, though objectively a dreadful picture ; but in over 90 per cent. of all the cases in which the cyanosis developed the course was progressively downhill towards death, the latter being preceded in many instances by delirium of a low type, associated with unconsciousness, though in some, on the other hand, consciousness was retained almost, if not quite, to the very last.

For a long time the nature and causation of this peculiar heliotrope cyanosis was obscure. It was certainly not due to cardiac or circulatory failure, for the condition of the heart and pulse remained strikingly good. At one time it was thought that there might be some peculiar chemical change in the blood leading to the formation of methæmoglobin, or even sulphhæmoglobin, but repeated spectroscopic examination showed no abnormal blood pigment to be present. Microscopical sections of the lungs, however, in which coagulative exudation both into the alveoli and into the interstitial tissues was often a very pronounced feature, showed that this albuminous exudate —quite different from that seen in ordinary pneumonic cases— was the probable cause of the cyanosis. The appearances in some lung sections were very similar to those of the profuse exudate that results from gassing, and layers of this albuminous fluid coming between the inspired air and the blood capillaries would necessarily interfere with the absorption of oxygen by the latter, and cause an extreme degree of anoxæmia. This was the generally accepted explanation of the condition.

The temperature was very variable. The ten charts indicate this. Five are from cases which recovered and five from cases which died. Sometimes the temperature dropped rapidly with speedy recovery, as in Chart I; but Chart VI shows that the temperature may seem to be falling comfortably by lysis and yet the patient may die. Chart II shows termination of the illness by crisis with recovery; Chart VII a similar sudden fall of the temperature followed by death; Chart III a fall by lysis

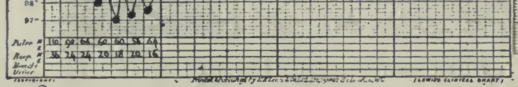


CHART I.

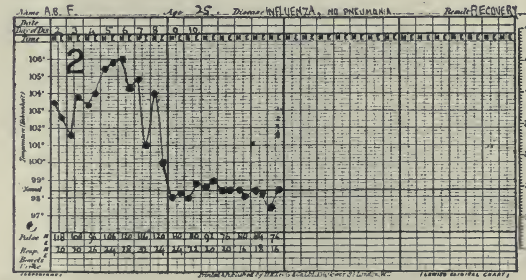


CHART II.

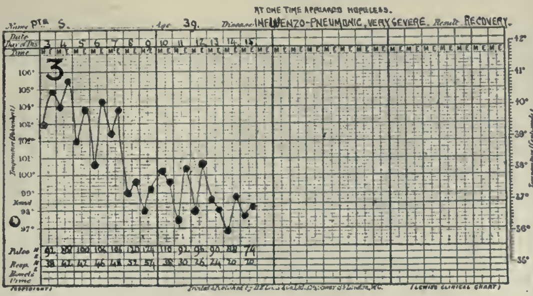


CHART III.

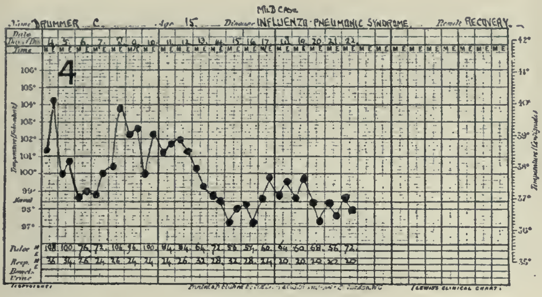


CHART IV.

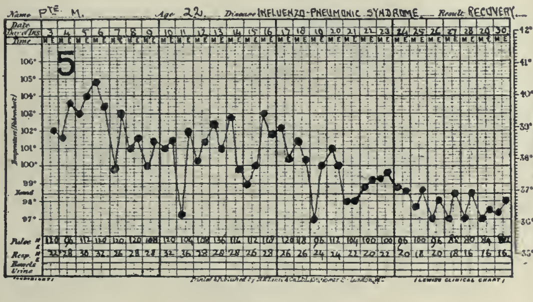


CHART V.

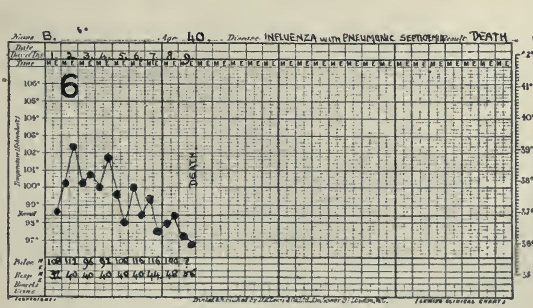


CHART VI.

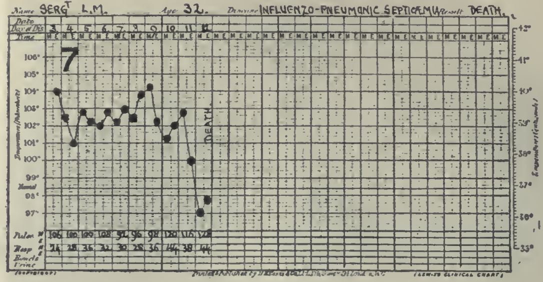


CHART VII.

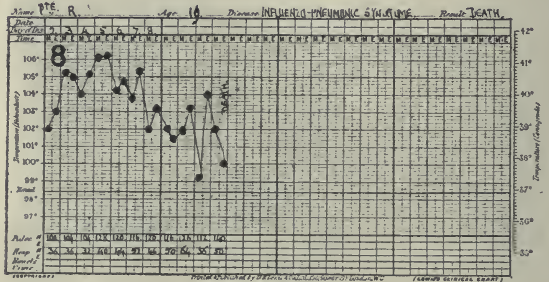


CHART VIII.

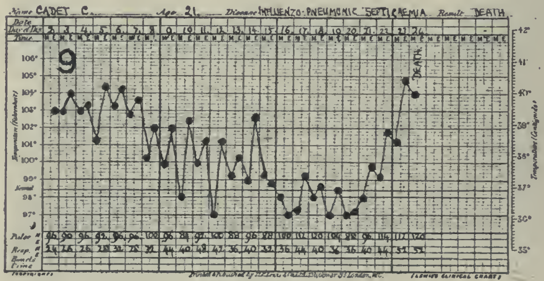


CHART IX.

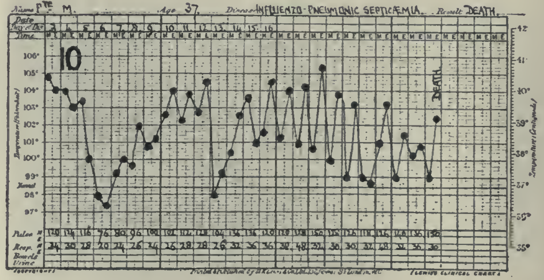


CHART X.

prolonged by irregular persistence for several days, ending in recovery; Chart IX a fall by lysis in a severe case that seemed to be doing well, with subsequent rapid rise and death. Chart X shows a rapid fall on the third day of the disease as though the patient had terminated his illness by crisis, but the pyrexia rose again by steps to a second maximum about the tenth day, when a second apparent crisis occurred, and yet the illness continued, pyrexia recurring after the second apparent crisis and terminating in death. While all varieties occurred, definite termination by crisis and recovery, as shown in Chart II, was very rare indeed. On the whole the temperature chart was of little use for prognosis.

The respiration rate was a much more helpful guide than was the pyrexia. The rapidity of breathing in the fatal cases was even greater than that in ordinary lobar pneumonia. Rates that were nearer 40 than 30 to the minute were very common, but in the worst cases the rapidity of breathing was generally over 40 and often 50 or even 60 to the minute, and this sometimes before the fatal cyanosis became evident.

The sputum was very variable. Some cases had hardly any sputum at all. Sometimes there was nothing but pure froth; again there might be froth only with some bouts of coughing, and nummular pellets of muco-pus at other times in the same patient; or the sputum might be glairy and mucoid, or stringy, or simply purulent. Again it might be tinged with blood streaks, or pure clotted blood might be coughed up separately, or there might be liquid red blood expectorated in a way recalling a moderate hæmoptysis from phthisis. Or the more purulent type of sputum might be tinged red or brown with altered blood, or it might be definitely glairy rusty sputum like that of ordinary lobar pneumonia. No conclusion could be drawn from the appearances of the latter as to what degree of the malady the patient had.

No ulceration of the stomach was found in fatal cases, but acute congestion was common. Bleeding per rectum was rare. A number of cases of spontaneous rupture of one or both recti abdominis muscles was met with, and in a still larger number this muscle was found at autopsy to be in a hæmorrhagic necrotic state, such as precedes rupture. Almost invariably this lesion had affected only that part of the muscle which is below the umbilicus.

Delirium and coma occurred in bad cases, but more striking was the number of cases in which they were entirely absent. Big, strong men, cyanotic, breathing 30 to the minute and obviously dying, would be fully conscious and would talk rationally, not realizing their danger in the least, to within half an hour of death. Subsultus tendinum was marked in many cases and was usually of bad prognosis.

Acute meningitis due to one of the infecting organisms found in other organs, *B. influenzæ, diplo-, strepto-*, or *pneumococcus*, occurred in a small number of cases. Acute otitis media with otorrhœa was rare, though temporary deafness and pain suggesting this condition were not uncommon. Of special importance in relation to the local pain behind the eyes frequently noted during the attack, and perhaps to the headaches which in some patients persist long after the acute illness, is the condition of the ethmoidal and sphenoidal sinuses described under the heading of morbid anatomy.

Albuminuria was common, and since in a total of over 100 autopsies there was no instance in which the kidneys were not definitely inflamed, the inference is that some at least of the albuminuric cases which survived had some degree of nephritis also. The number of cases in which permanent lesion has resulted is not yet known.

Jaundice was uncommon. Its degree and type were similar to those of the ordinary catarrhal form.

Unilateral or bilateral parotitis was not uncommon. It was exceptional for suppuration to occur.

Panophthalmitis was seen twice.

Pericarditis was occasionally reported. Endocarditis was not observed during the epidemic, nor was it seen at any autopsy, but it is noteworthy that throughout the year 1919 it was common to meet with cases of the chronic type of infective endocarditis whose origin was obscure.

Symptoms amongst Troops in the Field.

The incubation period lasted from two to four days according to various observers.

In the summer epidemic the onset was in most cases sudden. In a small minority it began gradually and reached its height within six hours. Rigors occurred in many cases. The initial symptoms were headache, pains in the back and limbs, and a feeling of weakness. In a report by Major Scarisbrick on 440 cases, the following relative frequency in the sites of pain was noted :—

Pains	in	the	head	occurred in	73	per cent.
,,	,,		back	,,	45	,,
,,	,,		eyes	,,	43	,,
,,	,,		limb muscles	,,	41	,,
,,	,,		knees	,,	32	,,
,,	,,		hips	,,	22	,,
,,	,,		ankles and shoulders rarely.			

Pains in the head and eyes, and pains in the back and muscles of the limbs were associated respectively. The pains were of a severe aching character. That in the head was referred usually to the frontal sinuses, that in the eyes to the back of the globe.

These initial symptoms lasted as a rule for two or three days ; the temperature commonly reached its height on the first, but sometimes on the second day. The highest level was usually between 102° and 103° F., but 105° has been noticed. In some cases the temperature never rose above 100°. It usually fell by lysis, but in a small minority a fall of three or four degrees was completed in twenty-four hours. In the First Army's Report of 18th June, the disease was called " three days' fever," and it was stated that the great majority of the patients were fit for duty in a week. But a week or two later it was found that many cases remained febrile till the sixth day. The pulse was rapid during the first two days, though it seldom reached 120, but was usually between 70 and 80 by the fourth day. At first there were hardly any other symptoms. On 12th June, Colonel Soltau, the consulting physician of the Second Army, reported :—

" There has been a remarkable absence of physical signs. In no case has the spleen been enlarged, nor has there been any rash. Rarely has anything abnormal been heard in the lungs, nor has there been any increase above the usual in the number of cases of broncho-pneumonia under treatment."

But a fortnight later he found that there had been an increase both in incidence and virulence, and mentioned the prevalence of pharyngitis with a tendency to spread down the respiratory tract.

Several symptoms of less importance were noticed. In some cases a rash was observed, usually of a mixed urticarial and erythematous character, principally seen on the neck, the shoulders, the wrists and the dorsum of the feet. This was noted also in Italy by Morelli, and in Germany. Labial herpes was sometimes seen, and became more common as pulmonary complications increased. Conjunctivitis and coryza were reported by several medical officers. Enlargement of the spleen was found occasionally during life, and has been reported *post-mortem.* The tongue, except for a clear marginal zone, was usually covered with a slight fur. This was grey or white, according to its degree, but the yellow or brown fur common in trench fever seems to have been rare. Anorexia was common. Loss of taste and loss of smell were observed. Vomiting was common in the first day or two, diarrhœa less frequent. At the commencement of the epidemic in May, several localized outbreaks were ushered in by vomiting and tenesmus in a majority of the cases.

Colonel W. E. Hume and Captain Todd at No. 42 Casualty Clearing Station noted the following relative incidence of symptoms :—

Headache and general muscular pain	76	per cent.
Shivering or definite rigors ..	41	,,
Suffused eyes	78	,,
Pharyngitis	100	,,
Furred tongue	100	,,
Constipation	52	,,
Spleen palpable	14	,,

In the earlier stages of the epidemic recovery was remarkably rapid, and convalescence was established without any sequelæ. The mental depression often associated in previous epidemics with a post-influenzal state was very rarely seen.

Towards the end of June 1918, however, the disease gradually became rather more severe. A short relapse of fever and symptoms about the seventh day began to occur and grew more frequent. Bronchitis, broncho-pneumonia, and lobar pneumonia began to appear. The two former were severe and prolonged, with a high irregular temperature, a rapid pulse, dyspnœa and cyanosis. The sputum was often of the green nummular variety. The few cases which resembled lobar pneumonia showed a more regular fever, but frequently terminated by lysis. Many cases proved fatal.

Pleurisy and pleural effusion occasionally occurred, and in one or two cases an inter-lobar empyema was found in which the *B. influenzæ* was the only infection.

A very few cases of pericarditis and suppurative otitis were noticed, but the chief complications after the pulmonary were albuminuria and nephritis. In some of the cases of nephritis, according to Symonds, a profoundly toxic condition supervened, with which were associated a dry, black tongue, pronounced mental symptoms, and a grey lividity of the face.

A rare complication was meningitis both of brain and cord, in which the *B. influenzæ* was found. In a few cases presenting similar symptoms, the cerebro-spinal fluid was found to be considerably increased, but to be sterile.

This wave of the epidemic died down at the end of July 1918.

The autumn epidemic which began at the end of September of the same year differed from that of the summer, chiefly in the increased proportion of pulmonary cases. Purulent bronchitis, broncho-pneumonia and acute pneumonia of the lobar type were all present. The temperature charts varied much. Some, and these were the most favourable, showed a high and level pyrexia falling by crisis as in pneumonia. Others with a similar high level fell by lysis. In others the temperature though high was irregular from the first. The two latter classes varied much in the duration of the primary fever. It sometimes fell at the end of a week, in other cases it persisted for three weeks or more. Some remained febrile for even six weeks. But the worst feature was the tendency to relapse. The fever would fall to normal and remain so for some days, and then, without any external cause, would rise again to its former height. A patient might recover from two such bouts and die in the third.

It was often possible at the time of the relapse to discover that a fresh part of the lung had been invaded, or that consolidation had taken place in a part where formerly only râles had been heard. But in other cases it was impossible to obtain any physical explanation of the recurrence of fever.

Even when the temperature fell and remained low, the lungs remained affected for a long time. The patient appeared to have no power to absorb the exudation or to recover his normal condition. It seemed that the infecting microbes had overcome his power to resist them. Many men died several days after their fever had subsided, and in nearly all it took many weeks before the lungs were free from signs of disease.

In many cases the patient was admitted in a state of cyanosis, which was not accounted for by the physical examination of the lungs. In some cases death occurred within the first few days, and while cases were described in which the *post-mortem* appearances showed little amiss, most of them showed extreme congestion, with a large amount of œdema fluid in the tubes and in the parenchyma. It may be said in general that the cyanosis was such as is hardly ever seen in ordinary hospital practice. Entering a ward, one might see six or eight of these cyanotic cases, some heliotrope, as it has been well called, others really purple, yet not appearing as much distressed in their breathing as might be expected from their colour. The opinion was expressed by some that such cases never recover. This was not true, yet no doubt on the whole it was a most unfavourable sign.

The explanation of this cyanosis was not easy. There was not in these cases such failure of the circulation as would account for it. In some instances the same may be truly said of the state of the lungs. The condition of congestion with œdema seen in others recalled phosgene poisoning, in which cyanosis is common.

The sputum was sometimes mucous, often purulent and nummular, often rusty. Not infrequently there was hæmoptysis like that of phthisis. Sometimes, on the other hand, there was little or no sputum.

The pulse in these cases was usually rapid for many days, and in some remained rapid after convalescence. The tongue, which in the early epidemic was almost always moist, became in bad cases dry and brown like the tongue of typhoid. Such patients fed badly, but many who fed well died. Indeed, one was struck by the fact that many died who almost up to the last ate well, slept well, and were in full command of their senses. Some, however, became restless and delirious, and closely resembled typhoid patients.

Pleurisy and empyema were not uncommon. Pleurisy with hæmorrhagic effusion was often seen.

Nephritis was a common complication. It occurred in a large number of the cases with pulmonary symptoms. The urine contained blood or albumin, sometimes in large amount ; the patient complained of pain in the back and for a time passed little urine. But there was little of the œdema which was a marked feature of the primary war nephritis. It was sometimes difficult to tell which the case really was. For instance, an officer was admitted for nephritis. He had blood and albumin in very large quantity in the urine, but he had no œdema, and he had considerable fever and marked signs in the lungs. Although his illness had not begun acutely, it seemed probable that it was influenza, and the opinion was given that the urine would soon become normal. It did so, but a fortnight later he again passed blood and again rapidly recovered. A similar attack occurred after exposure to severe cold two months later. The diagnosis lay between ordinary war nephritis with bronchitis, the febrile hæmaturia that was often seen in France, and influenza.

There was a marked tendency to hæmorrhage. Hæmoptysis has already been mentioned. Epistaxis was a common feature. Colonel Pasteur, the consulting physician of the Third Army, saw no less than 30 cases of hæmorrhage into the sheath of the rectus abdominis, and in cases reported by others this was found so large as in one instance to bulge into the abdominal cavity, and in another to rupture the sheath. A purpuric condition of the feet sometimes leading to the formation of blebs was also noticed. Hæmorrhages in the pleura and pericardium were frequently found *post-mortem*.

Jaundice had been seen on the American transport "Nestor" in September, but was infrequent in France until the beginning of 1919, when it became much more common. It occurred at all stages of the disease and was not of bad prognosis. In cases examined there was no obstruction in the ducts of the liver. The gastro-intestinal symptoms which in some countries were so marked as to differentiate a special type of the disease were not prominent amongst the British troops.

The white blood cells did not in uncomplicated cases present any significant variation in France. Leucopenia was found in 27 out of 100 German cases.

Pathology.

Although expert bacteriologists in various countries, who were thoroughly familiar with the appearance of Pfeiffer's bacillus and the technique necessary to demonstrate its presence, examined numerous cases in the first few months, they isolated bacilli in so small a percentage of cases that even those who recognised most fully that this latest pandemic reproduced in all essential particulars that of the early nineties, came to the conclusion that Pfeiffer's bacillus could at the most be regarded as associated with, but not as the essential and specific organism of influenza. And for a time its death-knell appeared to have been tolled when, one after another, Nicolle and Lebailly in Tunis, Gibson, Bowman and Connor at Abbeville, and Rose Bradford, Wilson and Bashford at Etaples, reported results which appeared to demonstrate the presence of a filterable virus capable of reproducing the disease in monkeys and the lower animals.

But as 1918 progressed, and as the different army laboratories became more expert in the technique necessary for the recognition of Pfeiffer's bacillus, steadily more and more observers reported the presence of this organism. More particularly, the bacillus was reported to be constantly isolated when " chocolate " medium was used—that is agar to which, when hot and just under the boiling point, blood or washed blood corpuscles are added, a medium so favourable to the growth of Pfeiffer's bacillus that within 24 hours large, easily recognisable colonies show themselves—and when swabs were secured from the upper air passages, or cultures made from the sputum in the early, as distinct from the late, stages of the disease.

Subsequently grave doubt was thrown upon the technique employed by those who reported the presence of a filterable virus. The criticism, it is true, did not explain away the statements of those who claimed that, employing the filtra from acute and typical cases of the disease, they had reproduced in monkeys what are admitted to be the characteristic lung lesions of the disease, namely hæmorrhages and œdema, and patchy peribronchial infiltration.

Thus at the end of the war there was no consensus of opinion regarding the bacteriology of the disease. Each of the following views had its upholders :—

1. That Pfeiffer's bacillus is the essential causative agent, the other organisms found in great numbers in the pneumonic lung of the fatal cases, streptococci hæmolytic and non-hæmolytic, pneumococci of the various types, staphylococci and gram-negative cocci being secondary invaders varying in their incidence in different regions.

2. That Pfeiffer's bacillus is not the essential causative agent, but either :—

(*a*) That like the streptococci and pneumococci Pfeiffer's bacillus is, during periods of epidemic influenza, so frequently to be found in the throats of those not affected with influenza, that even the fact of its being present in 100 per cent. of influenza patients would not prove it to be specific. Or—

(*b*) That the disease is due to the symbiotic or combined action of several organisms of which the *B. influenzæ* may be one, and streptococci or pneumococci most commonly the others. Or—

(*c*) That the essential cause is a filterable virus which in pneumonic and fatal cases most often paves the way for the growth in the respiratory passages of Pfeiffer's bacillus, and of sundry species of cocci.

While during 1919 small epidemics have occurred here and there, they have been of diminished virulence, with great reduction in mortality, so that, as in 1893, little opportunity has been afforded to any one individual to deal with an adequate amount of suitable material. Any predilection for one or other of these views must, therefore, be taken as the expression of an individual opinion and not as the commonly received view of bacteriologists in general.

There is the evidence brought forward by careful observers that the blood serum of influenza patients possesses a definite though slowly manifested power of agglutinating Pfeiffer's bacillus, which at the end of the first week rises from 1 in 50 to 1 in 80 according to various observers, the blood of normal individuals not agglutinating the bacilli in dilutions greater than 1 in 20. It is true that, as one observer points out, this reaction might show itself were the bacillus a secondary invader, true also that with complement fixation and absorption tests the results are irregular, indicating the existence of a great number of strains.

As regards the first objection, it is not an objection proper, only an alternative explanation. As regards the second, the same is true regarding *B. dysenteriæ*, yet this does not prevent one from regarding dysentery as a disease induced by various strains of the bacillus. One must however admit that the variation shown in Valentine and Cooper's New York results is extreme.

In the second place, there is the evidence afforded by vaccination, employing as vaccine *B. influenzæ* alone. Here the results at first appear to be very conflicting, but evidently everything depends on the mode of preparation of the vaccine. As pointed out by Duval and Harris, to kill off the bacilli by heat, after the method employed by Wright and Leishman in the preparation of typhoid vaccine, is futile. Even so low a temperature as 56° C. renders cultures practically worthless as an antigen. Tricresol and phenol derivatives also are not to be considered. Even 0.25 per cent. tricresol has a deleterious effect. Chloroform rapidly kills the bacteria without apparently having any harmful effect

Properly prepared with chloroform, the pure *B. influenzæ* vaccine was found by Duval and Harris to confer protection for from ten weeks to three months. Of 3,072 persons vaccinated, 2,608 with three injections, 346 with two, and 118 with one, 3·3 per cent. developed influenza, whereas among 866 unvaccinated controls the incidence was 41.6. Not one of the vaccinated developed pneumonia, whereas among the controls refusing vaccination there were 41 cases. Duval calls attention to the severity of the reaction induced by his vaccine. Constitutional effects following the administration were noted in 90 per cent of those inoculated, and in 30 per cent. they were severe and simulated in symptom complex the early toxæmia of true influenzal infection :—lassitude, severe frontal and occipital headache, neuralgic pains over the body, not infrequently ushered in by chills and nausea, and followed by a temperature of 101° to 102°.

And thirdly there are the observations upon the existence and actions of an endo-toxin by Huntoon and Hannum. These observers were unable to demonstrate the existence of a soluble toxin or ecto-toxin, but by growing 10 strains of the bacillus, drying the growths *in vacuo* and grinding them up with salt they were able to extract what apparently is an endo-toxin of which 0·25 c.c. was fatal to white mice, whereas similar salt extracts of meningococci, streptococci, and pneumococci were not fatal in four times the amount. The lesions induced by the bacillary extracts particularly involved the lungs, producing congestion with hæmorrhages.

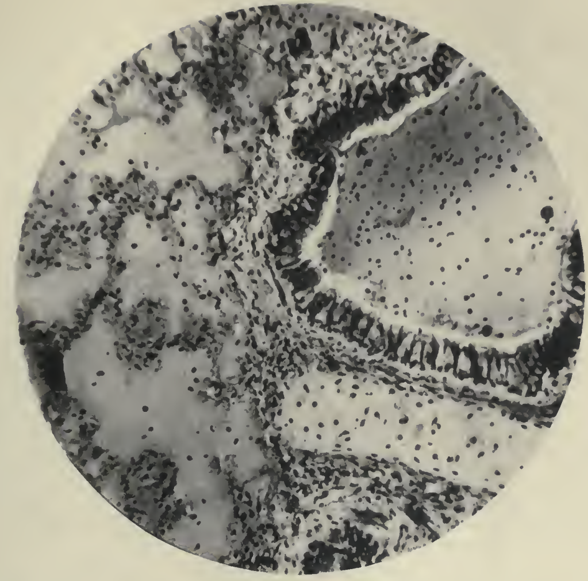
The latest strong evidence in favour of regarding Pfeiffer's bacillus as the specific organism of the disease comes from the army medical laboratory at Washington, where Major Blake and Captain Cecil, starting from the assumption that the pathogenicity and virulence of the *B. influenzæ* is rapidly lost in artificial media, proceded to raise the virulence by rapid successive passage through eleven white mice followed by thirteen monkeys. Intraperitoneal inoculations were given, and fluid was drawn from the peritoneal cavity from eight to ten hours after injection, that is, at a time when the bacteria were still actively growing in the cavity. The first and second cultures were employed for inoculation. The strain employed had been obtained six weeks previously from a child with influenza and pneumonia and at first had no virulence for white mice. After the eleventh passage, 0·01 c.c of a 16-hour blood-broth culture injected intraperitoneally killed a white mouse in 48 hours.

Twenty-two monkeys were next employed, some used for intraperitoneal injections and passage, the rest for infection through the respiratory passages, in part by swabbing or instillation through the mouth and nose, in part by direct intratracheal injection just below the larynx. Major Blake and Captain Cecil conclude that the disease initiated in monkeys by inoculation with these cultures of Pfeiffer's bacillus of exalted virulence appears to be identical with influenza in man; that when injected into the trachea the cultures produced in monkeys a tracheo-bronchitis and broncho-pneumonia, the pathology of which appears to be essentially identical with that which has been ascribed to pure influenza bacillus infection of the lungs in man; so that it seems reasonable to infer that *B. influenzæ* is the specific cause of influenza. (Fig. 1.)

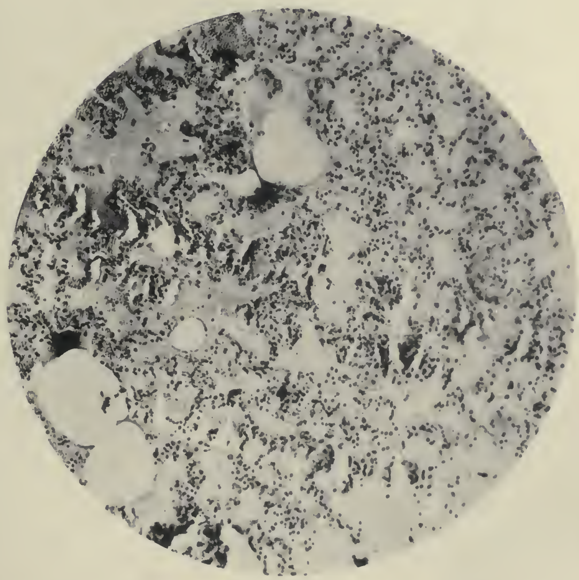
The question arises as to how these observations can be co-ordinated in the first place with those of the capable observers who have reproduced the lung condition by employing the filtrate from fluids obtained from influenza patients, but have failed to obtain cultures of *B. influenzæ* from the affected organs, or again with those observations of first-class observers employing the best methods, who, in localised epidemics which clinically were of the same disease, reported that 100 per cent. of the cases examined failed to afford influenza bacillus either by culture or by microscopic examination of the discharges or the lung tissue.

There is one possibility that cannot be passed over, namely, that Cecil and Blake employed mixed cultures of the influenza bacillus and an almost invisible virus. Another, that those who have failed to obtain the influenza bacillus from cases

Plate III.



A.—Monkey Lung (Group I, No. 4) showing inflammatory exudate in alveoli and bronchiole (mucous membrane intact) (x700).



B.—Monkey Lung (Group I, No. 6) showing margin of inflammatory exudate (left), clear lung (right) (x500).

which clinically were apparently identical, studied mainly old-established cases in which pneumonia had developed at a period when the influenza bacillus had been over-grown and destroyed by secondary invaders. These are points which have yet to be decided. It is worthy of note how frequently Cecil and Blake found the disease self-limited in the monkey, bacilli disappearing after the fourth or fifth day. In the meantime, however, one is impressed with the fact that the lesion common to mild and to severe and complicated cases is an acute congestion and inflammation of the trachea; that the one member of the characteristic group of minute bacilli of what is termed the influenza group, pathogenic in man, is the Bordet-Gengou bacillus of whooping cough, and that this also particularly affects and involves the epithelial lining of the trachea, as has been convincingly demonstrated by Mallory and his pupils.

It is true that the argument from analogy is dangerous, yet an arrest of the proper educent action of the ciliated epithelium of the trachea and bronchi, either by actual destruction and exfoliation of the epithelium, or, as in whooping-cough, by massive growth of the bacilli on the surface and between the cilia, affords the most satisfactory explanation of the frequent secondary infection of the lungs by organisms from the mouth and throat, with the development of forms of pneumonia varying according to the micro-organism which gains eventual dominance.

On the question of immunity it has hitherto been widely believed that a previous attack of influenza predisposes rather than protects. There have, however, been no accurate statistics, nor are there any on a sufficient scale now. A few reports from schools have shown a little evidence that those affected by the summer epidemic escaped that of the autumn. An analysis of the statistics of the war may throw some light upon the question. At present the only evidence worth considering is that provided by the preventive inoculation carried out in the army.

Morbid Anatomy.

The morbid anatomy of the disease presented a variety of pathological changes in the organs of the body. Autopsies were made in France during June and July 1918, by Captain Shore upon 30 cases in which the clinical diagnosis was "influenza." They illustrate the gross pathological changes met with and the frequency with which they occurred in the summer epidemic there. The patients were not all previously healthy for in seven cases, 23·3 per cent., obsolete tuberculosis, pulmonary or glandular, was found. In a previous series of 1,500 consecutive autopsies the total incidence of tuberculosis was 9·6 per cent. Two patients had chronic nephritis and one unilateral hydronephrosis. Old pleuritic adhesions were present in 12 cases. With these exceptions, the patients were apparently previously healthy. None were suffering from wounds. The most striking lesions were those in the lungs and heart.

In one form or another pneumonia was present in every case. The majority had broncho-pneumonia, which had a distinct tendency to become confluent, and to show a condition closely resembling the early grey stage of lobar pneumonia. Undoubted lobar pneumonia was only once found. In five cases the pneumonic areas were small and shotty when felt between the fingers, closely resembling miliary tuberculosis. On microscopic section the small patches were found to consist of consolidated lung, generally with fibrinous exudate, surrounding inflamed bronchioles. The name "bronchiolitis" was applied to the condition, but "miliary pneumonia" seemed more descriptive. No bacteriological investigations were made of these cases, so it is not possible to say if they differ from the more usual form of broncho-pneumonia in that respect. In two cases the process passed on from confluent broncho-pneumonia to abscess formation. Marked emphysema occurred in two cases, involving chiefly the anterior border of the lungs. In five there was an excessive amount of collapse, chiefly along the vertebral border of the lung. Two of these cases showed a small amount of pleural fluid, but in the other three the pleura was dry. Subpleural and interstitial hæmorrhages were seen in eighteen cases but only as small localized areas. Purulent bronchitis was present in fourteen cases.

Twenty-four cases showed recent pleurisy; fourteen of these were dry, but in ten a varying amount of purulent or sero-purulent fluid was found, never more than a pint and generally only a few ounces. In fifteen cases the bronchial or tracheal glands were markedly enlarged and inflamed. In a few cases more distant glands, such as the retroperitoneal and even inguinal, were affected.

One of the most striking features of the morbid anatomy of these cases was the constant occurrence of dilatation of the heart, accompanied by nearly as constant myocardial changes. Twenty-nine out of thirty cases showed marked dilatation of the heart, chiefly of the right side but very commonly of the left side as well, and twenty-one cases showed myocarditis demonstrable to the naked eye. The latter took the form of a general pallor and softness of the myocardium, with mottling and frequently subpericardial and subendocardial hæmorrhages similar to those seen beneath the pleura. These were not infrequently noticed on the interventricular septum, and on the papillary muscles. Endocarditis of the mitral valve was found in two cases. The vegetations were small and numerous, and obviously recent ; in one case there was a fair amount of recent thrombus adherent to the vegetations. In practically all cases the right side of the heart was distended with the yellow " agonal " or " chicken fat " clot found so constantly in pneumonia. Pericarditis was not found.

In most cases the spleen was a little enlarged. The largest weighed 15 oz., the smallest 4 oz., and the average weight of the series was 7½ oz. The spleen was generally pale and soft, and showed a marked enlargement of the Malpighian corpuscles. In a few cases it was congested. No infarcts were found.

The liver did not present any striking features. In most cases it was pale and inclined to show early fatty changes. Some few cases showed chronic or relatively chronic congestion, presenting a " nutmeg " appearance. In three cases a mild degree of jaundice was present, but there were no signs of biliary obstruction.

Apart from the two cases already mentioned as having chronic nephritis, ten cases showed a marked degree of " toxic nephritis." Sections were made of only two of these, but they showed no glomerular change, only cloudy swelling and a little fatty change in the tubules. In these ten cases the kidneys were flabby, pale and a little swollen. The capsule was easily removable without tearing the surface. Stellate veins were prominent on the surface. There appeared no divergence from the normal proportions of cortex, medulla, and intrapelvic fat. Their average weight was 12½ ozs. the pair, the average for the series being 12 ozs. In one case the kidney had a " flea-bitten " appearance, and on section showed, as well as the condition described, hyaline thrombosis of the afferent glomerular vessels. The glomeruli appeared to be practically all affected, which would account for the sudden and complete suppression of urine, without previous hæmaturia, which led to the patient's death. This was one of the cases which showed abscess formation in the lung.

Cerebral abscess was found in one case, in which purulent bronchitis but no particular bronchiectasis was present. Meningitis was not found.

Reports of 46 additional autopsies were contributed from various other pathologists in France. The predominating lesion was purulent bronchitis in 12, broncho-pneumonia in 29, and lobar pneumonia in five of the cases. In all but two cases the respiratory passages contained purulent exudate. In the two exceptions consolidation was of lobar type and confined to one lobe. In the cases with purulent bronchitis there appears to have been little or no consolidation. The commonest condition described is one of purulent bronchitis with broncho-pneumonia often associated with fibrinous exudate upon the pleural surface. The lungs are described as greatly congested and as exuding blood-stained watery fluid from the cut surface. The extent of the broncho-pneumonic areas varied from numerous areas a few millimetres in diameter, surrounded by regions in which hæmorrhage had occurred, to confluent broncho-pneumonia involving the greater portion of a lobe. Sections of the lungs showed the same irregular patches of consolidation with alveoli filled with leucocytic exudate or blood and often interspersed with emphysematous portions. The surrounding vessels were greatly distended, and the mucous membrane of the bronchioles swollen and disintegrating. Pneumococci were seen in the alveoli amidst the leucocytes, and sometimes in immense numbers, but in only a few instances were bacilli resembling Pfeiffer's bacillus recorded.

Cultures were made from the broncho-pneumonic areas in 53 instances. Pneumococci were invariably recovered, and in 40 cases bacilli resembling *B. influenzæ* also. Similar bacilli have been isolated from the meninges in cases dying with meningitis and, along with pneumococci, from the fibrino-purulent pleural effusion.

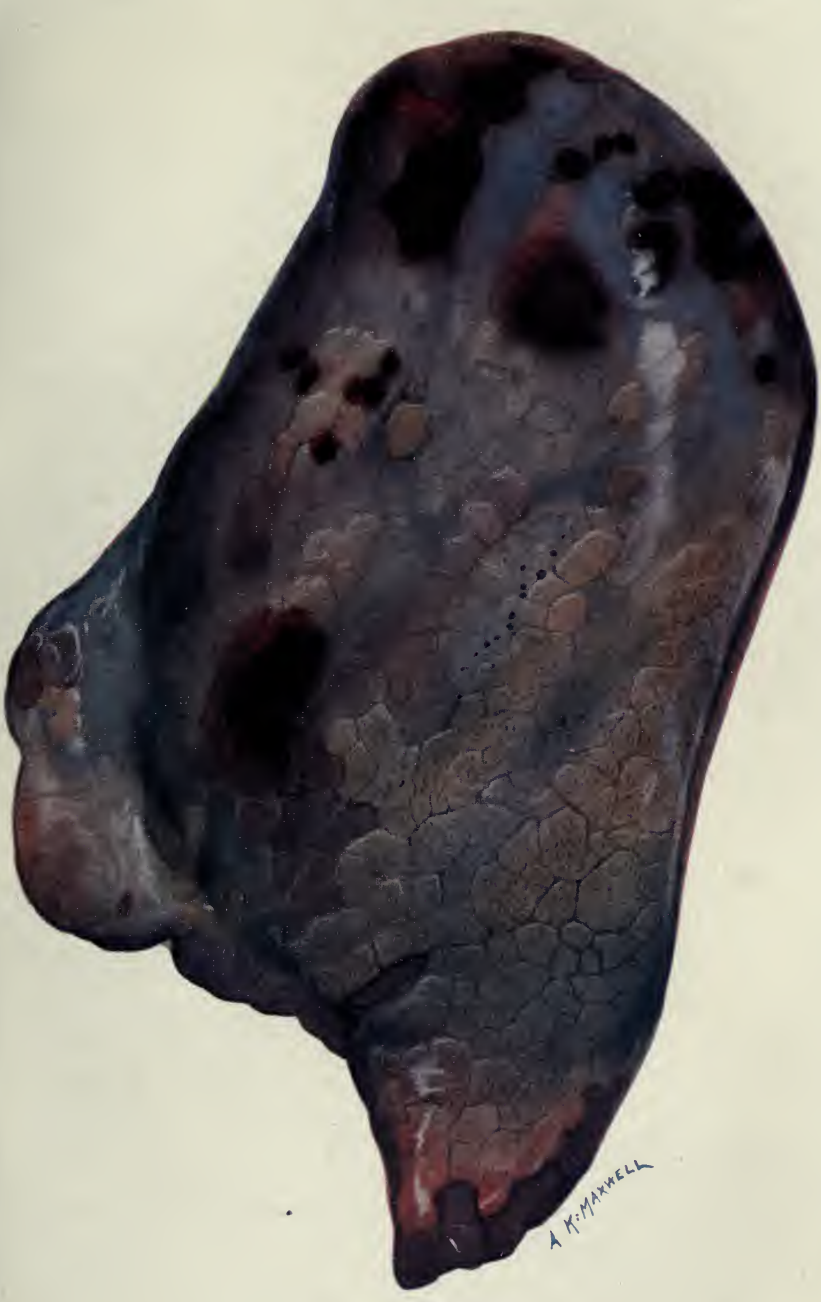
The only lesions in other organs recorded were congestion of the kidneys with small hæmorrhages in the pelvis of the kidney. In one instance small hæmorrhages in the white matter of the brain were observed.

Autopsies made in England during the summer and winter confirmed these observations and amplified them in the following directions.

In 22 consecutive cases the results of examination of the cranial sinuses were as follows :—One case was normal, in 21 cases the lining membrane was congested, in 6 there was definite yellow pus, in 15 turbid fluid yielding in every case the same micro-organisms as were found in the lungs. To the naked eye the ethmoidal sinuses were less affected than the sphenoidal, and the frontal least of all, but there was little difference in the results of culture.

The lesions found in the lungs included acute congestion, giving a more or less dark red colour to the whole lung ; diffuse hæmorrhage producing still darker red, often almost black-red areas in the already deep-red lung, varying in size from miliary

Plate V.



WHOLE LUNG IN A CASE OF INFLUENZAL PNEUMONIA.

to massive, and scattered at random throughout the lungs; hæmorrhagic infarcts similar in colour to diffuse intrapulmonary hæmorrhages, but differing from the latter in their pyramidal shape; broncho-pneumonia, sometimes recognizable only on careful search, sometimes widely disseminated, and occasionally confluent; miliary abscesses, often aggregated together in little focalized groups of from three or four to a score or more, similar to those seen in the midst of septic infarcts due to infected emboli; croupous pneumonia, met with very rarely indeed; purulent bronchiolitis, with thick pus expressible from the bronchioles seen in the cut lung; collapse, sometimes superficial only, sometimes associated with multiple areas of broncho-pneumonia, sometimes massive; passive œdema of the bases; active œdema with extensive albuminous exudate into all parts of the lungs, not definable by the naked eye, but shown to be extreme in many histological sections, a peculiar and apparently highly important feature of these cases; and interstitial emphysema, often widespread throughout the lung tissue.

It is worthy of note that here and there a case occurred with the same clinical picture as the rest and yet with lungs so little altered to the naked eye that one might easily have passed them as almost normal. Microscopically there would be bronchiolitis, peribronchiolitis and diffused inflammatory albuminous exudate, both interstitial and intra-alveolar, yet without any discernible broncho-pneumonia, and no obvious consolidation anywhere. No part of any lobe, larger than a minute fragment, would sink in water, and yet the clinical picture of the case was indistinguishable from that in which extensive broncho-pneumonia would be found at autopsy. In short, though broncho-pneumonia was usually found in little or greater degree, it was only part, but not an essential part, of a much more complex mixture of lesions.

Microscopically the lung lesions were found to be just as protean as the macroscopic appearances would suggest. The most remarkable were the "Gruyère cheese" changes, which were common and entirely unlike what is met with in any ordinary form of pneumonia. The condition has been illustrated in the special report series* of the Medical Research Committee, and it is not very dissimilar to the initial results of the action of acute irritant gases on the lungs (Plate V). All through the section of the lung—filling the alveoli in some places, distending the interalveolar walls or the peri-bronchial connective tissue in others, or blocking the bronchioles, or infiltrating all parts of the section simultaneously—there was a hyaline or homogeneous material, staining faintly pink with eosin, but containing few cells, resulting apparently from the rapid outpouring of an albuminous, non-cellular, coagulable exudate which in the process of fixation of the tissues becomes converted into what looks like hyaline material. (Fig. 2.)

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* No. 36.

Amid this are seen outlines of normal alveoli in some places, alveoli whose walls are disintegrating in other places, and, in yet others, spaces which are not alveolar at all, round or ovoid holes of varying sizes without any defined walls, but reminiscent of the air holes which characterize a Gruyère cheese. Some of these may be the result of breaking down of interalveolar walls so that two, three or more original alveoli have been thrown together into one larger one. Some, on the other hand, appear to be gas-bubbles—microscopic interstitial emphysema—in the albuminous intrapulmonary exudate. Similar non-cellular exudate is seen after acute gas poisoning. It seems likely that it is this acute inflammatory œdema of the lung tissue which, preventing inspired air from gaining access to the intra-capillary blood, accounts for the anoxæmia and heliotrope cyanosis of the worst cases.

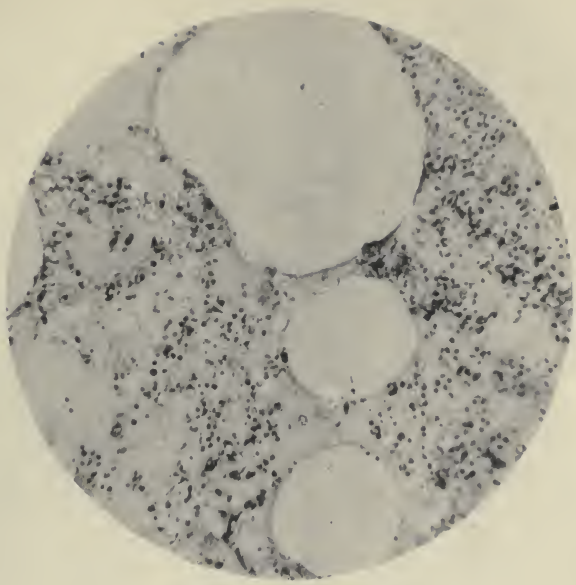
The lesions found in the lungs may be summed up as consisting of bronchitis, usually of the severe purulent type; hæmorrhagic œdema, especially in cases rapidly fatal; and inflammation and consolidation of the parenchyma, which may be miliary or lobular, sometimes so confluent as to involve large areas, but is rarely true lobar consolidation. Microscopically the characteristic change is that of vacuolation with fibrinous exudation.

The thyroid gland was uniformly enlarged in nearly every case, a phenomenon which attracted attention, though its causation was not obvious. The gland was sometimes quite three times the average size, and the isthmus was swelled as well as the lateral lobes, much in the same way that it is in Graves' disease. The swollen gland was firm and uniform in consistence, generally of its ordinary dull-red colour, and microscopically it did not show evidence of being acutely infected. The condition seemed to be one of simple uniform swelling of the gland secondary to the acute toxæmia of the general disease.

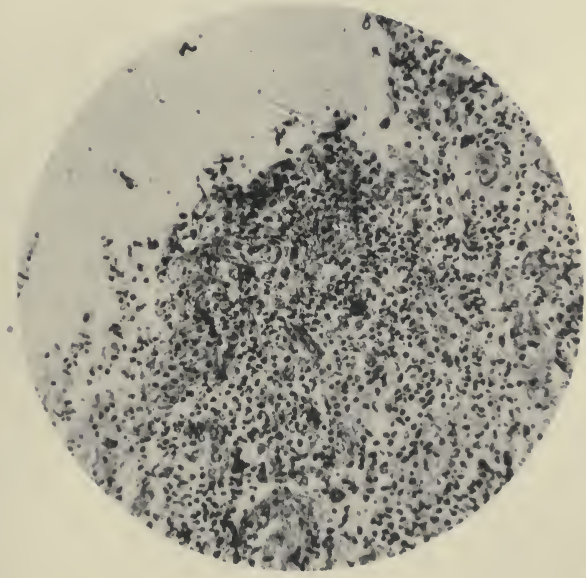
The alimentary canal seldom presented microscopic evidence of infection; but a group of cases was observed in which the colon was in a state of extensive and acute ulcerative colitis, with destruction of the mucosa similar in type and degree to that which results from acute dysentery.

Important investigations into the pathology of epidemics

Plate IV.



A.—Human Lung, area of oedematous pneumonia, showing alveoli filled with albuminous exudate. Leucocytic reaction not marked. (x700).



B.—Human Lung, area of multiple abscess formation, showing total destruction of bronchial mucous membrane with rupture and solution of the surrounding alveolar walls. (x700).

of pneumonia, which occurred in the army concentration camps in America during 1918, have some bearing on the epidemics of influenza. A full account of the work has been written by MacCallum in a monograph of the Rockefeller Institute and in other papers.

MacCallum points out that, during the period referred to, examples of the classical type of lobar pneumonia, ending by crisis, were met with in the usual numbers to be expected under camp conditions and at the season of the year in which they occurred. There arose, however, in addition, outbreaks of pneumonia of a very different character, which appeared to follow in the train of other epidemics of some predisposing disease of which measles and epidemic influenza were the chief. It is in its ultimate application to the epidemics of influenza that the work of the American pathologist requires particular attention. During the winter and spring 1917–18 there were extensive epidemics of measles in the American camps, complicated by a very fatal pneumonia shown to be due to the invasion of the lungs by a hæmolytic streptococcus. During the great epidemic wave of influenza in the latter part of 1918 similar pneumonic complications were observed, and in these the secondary infecting organisms were observed to be the hæmolytic streptococcus, the bacillus of Pfeiffer, and *Staphylococcus aureus*. MacCallum showed clearly that there were important differences in the pathological pictures of these various pneumonias, and that they depended on a variety of factors, such as the nature of the predisposing or primary disease; the organism which secondarily invades the lungs; the virulence of the organismal strains; and the resistance of the infected person.

Though it is possible to describe typical appearances as brought about by a single variety of invading organism, such a clean picture is not commonly met with. The various secondary invaders may all be present, or they may invade the lungs one after the other, and each produce additional effects. It is, however, common for one or other of the organisms to multiply quickly, and assume a predominant rôle in the pathology. Subsequently another organism may multiply, and add to, or even completely cover up, the lesions produced at the earlier stage. All these changes increase greatly the difficulty of elucidating the pathology of different ætiological types of the disease. It should be mentioned that MacCallum assumes that in the present state of knowledge neither of the main predisposing diseases, measles and epidemic influenza, can be considered as caused by bacteria, but that they must be ascribed to a virus of unknown nature.

The first epidemic of pneumonia investigated by MacCallum occurred during a great outbreak of measles in a Texas camp in February 1918. In this epidemic the main secondary invader which brought about the pneumonia was clearly shown to be a hæmolytic streptococcus. So obvious did this become that ultimately the prophylactic measure was adopted of segregating all cases of early measles in which the hæmolytic streptococcus could be obtained in the throat. This was followed by excellent results in diminishing the pneumonia incidence in other cases of measles.

A later epidemic in another camp occurred without the co-existence of measles at all, from the bulk of which again the hæmolytic streptococcus was obtained. In this epidemic the streptococcus was apparently virulent enough to set up pneumonia without the usual primary predisposing disease coming into play.

The characteristic lesion of all these cases may be summarized as being that of an *interstitial* broncho-pneumonia of an unusual type. Macroscopically the cut surface of the lung showed branched grey projecting foci of consolidation, surrounded by areas of œdema, hæmorrhage and collapse. The essential feature of the lesion on histological examination was the rapid infiltration of the walls of the alveoli and bronchioles with wandering cells, followed by new formation of connective tissue in these situations, so that the walls of the alveoli become greatly thickened. The streptococci were present in the lesion in relatively small numbers, and were confined practically to the bronchi and lymphatic channels of the lung. This is in great contrast to the findings in lobar or lobular pneumonia, where the main lesion consists in exudation of fibrin and leucocytes into the alveolar spaces, and where myriads of pneumococci or other organisms are to be seen in the alveolar exudate. The peculiar acute inflammatory change in the alveolar walls, with cellular infiltration followed by fibrosis, appears then to be a particular pathological change characteristic of the disease caused by the hæmolytic streptococcus after measles.

The appearances varied somewhat according to the stage at which death occurred. In cases where death supervened within a few days of the onset, no actual areas of consolidation were seen on the cut surface of the lung. All the bronchi were intensely reddened, and their walls were swollen. Microscopically such a lung showed in the bronchi an accumulation of leucocytes containing streptococci. The damage extended beyond the bronchi only into the closely adjacent alveolar walls, which were thickened by œdema and infiltrated by mononuclear wandering cells. If the illness had lasted more than a week, the post mortem changes were far more advanced. There was then generally pleural exudate, thin, watery and turbid, often with a greenish brown sediment, and swarming with streptococci. The lung surrounded by the fluid exudate was collapsed, airless and flabby, but contained obvious palpable areas of consolidation. In section, the lung surface showed nodules of consolidation which projected above the cut surface and were surrounded by areas of hæmorrhage and œdema. Each bronchus contained thick pus. The infection was essentially confined, in the first place, to the interstitial tissues either of the wall of the bronchioles or of the alveoli, and the organisms showed a tendency to pass from these areas to the surface of the lungs by the lymphatic drainage channels, which in consequence might be distended with such large collections of pus as to resemble a choked bronchus. Microscopically the same interstitial changes were predominant, but further advanced. The interlobular septa were greatly thickened, and the alveolar walls were thick both from infiltration with wandering cells and from the formation of new connective tissue, which was well vascularized. The alveolar spaces might contain at this stage dense plugs of fibrin, mixed with catarrhal cells from the alveolar walls, but leucocytes and red corpuscles were scanty.

In certain cases the familiar lesion of lobular pneumonia was also present in other parts of the lungs, the alveoli being filled with exudate of fibrin and leucocytes containing in the meshes very abundant streptococci. This change MacCallum regarded as evidence of lowered resistance on the part of the host, so that there was no restriction to the invasion and multiplication of the streptococci. The alveoli became filled with organisms in contrast to the course of events in the interstitial pneumonia where the organisms were "imprisoned in the bronchi, and carried to the pleura only by migration along the lymphatics."

In these epidemics MacCallum found that all the cases could be divided pathologically into the following types :—

(1) Lobar pneumonias caused by the pneumococcus.

(2) Pneumonias caused by the hæmolytic streptococcus, either pure interstitial broncho-pneumonias, or interstitial pneumonia added to lobular pneumonia, or rarely lobular pneumonia without any of the changes in the framework of the lung.

MacCallum's subsequent work refers to the pneumonias met with during the great influenza epidemic in the autumn of 1918. He again affirms that the nature of the primary disease is unknown, but that it *lowers the powers of resistance to a degree scarcely paralleled in any other disease.*

In this epidemic the secondary pneumonia was brought about by invasion of the lungs with many kinds of bacteria, including the various types of the pneumococcus, the staphylococci, and the bacillus of Pfeiffer, invading singly or all together.

The type of pneumonia was here again found to be quite different in different epidemic areas in America, according to the predominant secondary invading organism.

In the cases where the various types of pneumococci were identified as the predominating organism, the consolidation was seen to be at first lobular, but soon these solid areas coalesced until the greater part of a lobe might be solid and airless. The bronchi in these cases were not red, but pale. Microscopically the aveoli were found filled with a light fibrinous reticulum, entangling red corpuscles, leucocytes and desquamated endothelial calls. This exudate contained as a rule abundant pneumococci, and in fact the lesion was very little different from a typical early lobar pneumonia.

In the cases where the hæmolytic streptococcus was the chief secondary invader, the appearances in the lungs corresponded to those described in the earlier epidemic as characteristic of the invasion of tissues in cases with lowered resistance. None of the typical interstitial connective tissue changes were present, but there were large areas of lobular consolidation packed everywhere with streptococci, and often undergoing rapid necrosis. In these cases again intense inflammatory redness of the trachea and bronchi was evident.

The few cases in which the staphylococcus appeared to predominate were too scanty in number to give absolute conclusions, but in one the lesion was similar to that induced by the pneumococcus.

In the cases in which Pfeiffer's bacillus was present in abundance the changes found resembled very closely those described as acute interstitial pneumonia caused by the streptococcus after measles infection. There was again the same thickening of the alveolar walls with round-celled infiltration and newly formed connective tissue, while the small bacilli were practically confined to the bronchi and did not invade the alveoli. It was evident from the lesion that the tissues here were stoutly resisting the invasion of the bacilli.

MacCallum concludes one of his papers by saying that stress must be laid on the *epidemic character of the secondary invasion of the lungs* in all the outbreaks. In one camp all the pneumonic cases might show a pneumococcal type of lesion, in others almost every case might be due to Pfeiffer's bacillus. In this way Pfeiffer's bacillus might carry conviction to some people as the true cause of epidemic influenza, whereas it might be almost absent in other areas where pneumococci and hæmolytic streptococci were the opportune secondary invaders. This all leads him to the reiterated conclusion that we are still quite ignorant of the cause of epidemic influenza.

Acute interstitial pneumonia was recognized microscopically in France by Dunn and McNee in December 1916, in individual cases of "broncho-pneumonia" before the influenza epidemic. The general observations of MacCallum and Cole in 1918 were fully confirmed during the epidemic by Tytler, Janes and Dobbin in work at Boulogne; in these latter cases staphylococci were frequently present among the secondary infecting organisms, and staphylococci were especially prominent in a group from Malta, recorded by Captain Patrick.

Diagnosis.

With regard to diagnosis, influenza has to be distinguished from the onset of any other acute fever. In the case of the zymotics the subsequent course and the rash proper to each form the main points of diagnosis. Trench fever can sometimes only be distinguished by its relapsing character as the rash may be inconspicuous. Severe influenza may closely resemble typhoid fever; in this case the diagnosis turns upon the presence of the signs of the latter disease. Some regard a relatively slow pulse as characteristic of severe influenza, but this may occur in typhoid also, and is not universal in cases of influenza. Malaria may resemble influenza. The history and the presence of the malarial parasite will usually provide grounds for diagnosis.

Prognosis.

The prognosis of the disease is indicated in the descriptions of its symptoms and progress. Inquiries made seem to show that the epidemic has not produced any large number of those mental sequelæ which have been noticed on previous occasions. There is some suspicion that a rather chronic form of infective endocarditis may be the consequence of an attack of influenza. Also it is said there are some cases of fibrosis of the bases of the lung resulting from the epidemic. It is suggested above that the kidneys may be left affected. Such cases are not, however, numerous.

Treatment.

The treatment of influenza is both preventive and curative. Segregation was attempted in France On 23rd June, 1918, a committee appointed to investigate the outbreak reported to the D.G.M.S. as follows :—

> "1. The contagion of this disease appears to be air-borne, although its exact nature has not yet been ascertained. The main principle to be followed, therefore, is to spread troops as widely as possible, avoiding the crowding of men in tents, billets, messrooms, etc.
>
> "2. Whenever the military situation permits, it is advisable that troops should sleep in individual blanket-shelters in the open air.
>
> "3. As the infection appears to be spread by the movement of infected individuals, drafts arriving at reinforcement depôts from England or the bases should as far as possible be accommodated in separate lines for a period of four days. Individual shelters should be insisted on, in order to avoid the necessity for quarantine if any cases arise.
>
> "4. In medical units arrangements should be made for the separation of these cases from other patients.
>
> "5. In billets where infection has occurred all blankets and kits should be taken out and aired, and the usual precautions taken so far as circumstances permit."

Later a further segregation was made by separating cases of broncho-pneumonia from the remainder.

In most influenza wards the nurses and orderlies wore masks. The incidence of infection among them was on the whole surprisingly small, but it can hardly be attributed to the masks, which were carelessly used, for it was small too even in those wards where masks were not worn.

In Mesopotamia, where the disease was recognized, its incidence was so great that the hospitals were overtaxed. In the 15th Indian Division regiments were ordered to form their own hospitals and detain cases. Tents were set aside, latrines made, personnel detailed for nursing, water and cooking arranged, and drugs and comforts supplied. For prophylactic purposes games were stopped and units were paraded twice daily when every man gargled his throat and inserted in each nostril some menthol and camphor ointment.

Preventive inoculation was employed to some extent. Eyre and Lowe in England had some time before inoculated a body of New Zealand troops with a mixed vaccine against respiratory diseases. These troops during the following six months showed as compared with unvaccinated New Zealand troops a rate of respiratory disease lower in the proportion of 12 vaccinated to 73 unvaccinated of those attacked. A War Office conference reported in favour of a prophylactic vaccine containing :—

B. influenzæ	..	60 millions	in 1 c.cm.
Pneumococci	..	200 ,,	
Streptococci	..	80 ,,	

the first dose to be ½ c.cm., the second, to be given 10 days later, 1 c.cm. But both dosage and composition were criticized by Matthews and Wynn. Eyre and Lowe again reported favourably on their results during the autumn epidemic.

In the autumn epidemic in France it was considered inadvisable to use the prophylactic vaccine upon the combatant troops, as it was impossible to be sure that men were not already infected, and there was some evidence that a negative phase was produced which might in that case be dangerous, but at Boulogne a test on a small scale was made on the base personnel with equivocal results.

Prophylactic vaccine did not arrive in Mesopotamia till April, by which time the epidemic had so far died down that no satisfactory trial of its use could be made.

Leishman's statistics, published in 1920, show a much lower rate of incidence among those previously inoculated with this vaccine. Further, among 221 inoculated patients who caught influenza only two died, whereas among 2,059 non-inoculated patients 98 died. The numbers included in his returns are approximately 60,000. There are one or two anomalous returns, and there are one or two which appear unreliable. Expert statisticians also claim that the circumstances of infection diminish to a certain extent the difference between the rates. Yet a balance of evidence is left in favour of inoculation as a means of preventing the disease, and the low death rate of the inoculated affords considerable evidence of the creation of temporary immunity.

It was, however, considered advisable to increase the proportion of *B. influenzæ* and the vaccine eventually issued by the War Office contained :—

B. influenzæ	..	400 millions	in 1 c.cm.
Pneumococci	..	200 ,,	
Streptococci	..	80 ,,	

the first dose in ½ c.cm., and the second, 1 c.cm., as before.*

---

* Extreme measures of protection against the pandemic of influenza in 1918 were taken on board the Japanese cruiser "Nukata," which was in Simon's Bay and Table Bay during the progress of a very severe and fatal outbreak in the Cape Peninsula during the latter part of the year. The personnel of the ship entirely escaped infection. The preventive measures included stoppage of shore leave or of visitors from shore, the wearing of masks by men necessarily sent on duty on shore, disinfection of everything taken on board and inoculation with anti-influenza vaccine. Vegetables from the shore were washed and exposed to sunshine; bread was exposed to heat in kitchen ovens, meat and fish were exposed to air and the covers on them changed on the pier at Cape Town; newspapers and letters were sprayed with formalin and dried in the sun; men returning from shore duty gargled with 1 in 1,000 solution of perchloride of mercury and cleansed their clothing and boots with a 3 per cent. solution of carbolic acid on the pier before returning to the ship. They were given formalin tabloids to use on shore and instructed to avoid crowds. The men on board gargled with salt after every meal and with perchloride of mercury solution before turning in. Temperatures were taken every day and men with signs of inflammation of the naso-pharyngeal passage searched for and isolated. All table dishes were boiled after use and at the height of the epidemic on shore no provisions from shore were allowed on board. (See Vol. I. General History of the Medical Services, p. 319.)

Preventive inoculation with mixed vaccines has been tested in New York, on 6,000 persons by Jordan and Sharp, and on over 4,500 by Park, with doubtful result. The dose of influenza bacilli was 500 and 1,000 millions in their respective vaccines.

With regard to curative measures alike in France and in England treatment was mainly symptomatic. There were not wanting, however, advocates of specific remedies.

Turner advised 20 grain doses of salicin every hour, and stated that out of 2,500 cases thus treated he had lost none, and had never seen bronchitis or pneumonia develop. In France the cases came in too late to give this method a trial, and there has been no corroboration of his statements on a large scale in England. Quinine and the salicylates were of little use. Corrosive sublimate and colloidal arsenic or silver, the former recommended by Ferrarini in 1 cgm. doses, the latter by Capitan, as intravenous injections, were each praised by some officers, whose reports were controverted by others. Large doses of alcohol were ineffective. Oil of camphor and musk were advocated as restoratives. The usual expectorants were given. Cyanosis was temporarily relieved by oxygen inhalation through the Haldane apparatus. Oxygen was of about as much value as it is in cases of ordinary lobar pneumonia and, whereas in gas poisoning it undoubtedly saved life and that frequently, in influenza it at the most sometimes prolonged it. Venesection is never permissible.

Treatment by the serum of convalescents advocated by Benjafield and Hohlweg was not tried in France. Its efficacy depends upon the degree of immunity conferred, which is yet uncertain; but further trial is very desirable, for clinical evidence, though difficult to estimate, is in such a case the final test. Curative vaccine treatment was not employed in France, and was not found of value by those who tried it in England.

The points of main importance are that a patient with influenza should be sent to bed at once, and should not be sent long journeys if these can be avoided ; yet even when these precautions were taken and the best possible conditions secured throughout, experience showed that the attack might be very severe.

At Aldershot the overcrowding was so great that the most hopeless cases were placed under shelter in the open air, to make room in the wards for those whose chances seemed more favourable. It was found, to the surprise of the physicians, that an unexpectedly large number of these apparently hopeless cases recovered, though it was winter time. This accidental observation may be of great importance, and the open-air method should certainly be tested again.

Empyema was uncommon in France, and is not even mentioned in the account of the disease in England, but it seems to have been more frequent in the American army. It should be borne in mind, and, when found, should be treated first by aspiration, and, if it collect a second time, by resection.

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CHAPTER VIII.

PURULENT BRONCHITIS AND BRONCHO-PNEUMONIA.

DURING the campaign in France and Flanders respiratory affections were common, and at certain periods the numbers affected were large, more especially during the cold and wet seasons. These maladies were of the usual and well-known types, such as bronchitis, pleurisy and varieties of pneumonia, and they do not call for special notice. They varied in their severity and character and in their incidence amongst the troops, derived as they were from different parts of the world and often of different races. Such affections were prevalent from time to time during the earlier years before the occurrence of the pandemic of influenza in 1918, and in some years, notably in the winter of 1916, they assumed considerable proportions. In 1918, however, they occurred in very large numbers in association with the severe epidemic of influenza prevalent in the autumn of that year.

Bronchitis was one of the diseases that occurred, as might be expected, in different degrees of severity and in varying numbers in different years, and it also presented varying forms, sometimes catarrhal, sometimes muco-purulent and not uncommonly frankly purulent. Such varieties are well known and universally recognised. But, in addition to these, another and remarkable form of the disease was seen from time to time in isolated instances, and, in certain years, in considerable numbers. It is this variety of bronchitis to which the term acute purulent bronchitis is given. The outstanding features of the malady are the remarkable and peculiar sputum, the high fever and prolonged course of the disease and in a certain proportion of cases tachycardia. Other striking features such as cyanosis, and the patient's mental state, although also of much clinical interest, are phenomena that are by no means unusual in other severe forms of bronchitis, especially when acute, and hence although they are prominent features of purulent bronchitis, they are not so special as the sputum and the prolonged and high pyrexia.

In France, although sporadic cases were seen from time to time throughout the campaign, the bulk of them occurred in the winters of 1914 and 1916, while very few were seen in the winters of 1915 and 1917. In the autumn and winter of 1914 the weather was cold and very wet and the troops suffered considerably from exposure. The winter of 1916 was also severe; the malady was then more prevalent but the number of men serving was much greater than in 1914. The remarkable feature is rather the fact that so few cases occurred in 1915. In addition to the cases occurring in healthy men, purulent bronchitis was not an uncommon complication in the wounded, and many cases were seen as complications of chest wounds, especially where the wounded men had not been picked up until the lapse of some time. Hence it seems that exposure was a factor of importance in the causation of the disease. It is of interest that although the bacillus of Pfeiffer was the organism most constantly found in the sputum, the disease occurred in the years 1914 and 1916, when there was no epidemic of influenza in the armies.

The disease attacked strong, healthy men, and although most cases occurred in the more mature men, some were seen in quite young soldiers, and the disease was by no means one which chiefly affected the older men. This was more especially seen in 1914 and 1916, when the ætiological problem was not complicated by the presence of the influenza epidemic. The 1914 cases occurred in the men of the old army, and the 1916 in the men of the new armies, and both these categories were exceptionally vigorous and strong men. The influence of cold and exposure in causing the development of this more virulent type of bronchitis was very evident among men who came from India to Flanders during the winter of 1914–15, and naturally felt the climatic conditions more severely than did the relatively acclimatized troops from home. Certain British battalions, which were recalled from India and arrived for service in France in December, suffered severely from the disease. Indian troops serving in Flanders were similarly affected.

Hospital returns never made a reliable differentiation between purulent bronchitis and other respiratory diseases, but the following figures for 1914 and 1915 from the Meerut Stationary Hospital, at Boulogne, serve to illustrate the frequency of these maladies amongst Indians :—

Total admissions	20,107
Respiratory diseases	2,485
Deaths from latter	84

These cases included 233 returned as pneumonia, with 58 deaths; and in many the pneumonias were in reality cases of purulent bronchitis.

The incidence of similar types of disease amongst troops in the United Kingdom was first brought to notice early in 1916, when Major Abrahams and Colonel French observed at the

Connaught Hospital, Aldershot, that certain cases admitted as "pneumonia" differed very materially from any ordinary cases of lobar pneumonia in the paucity of their physical signs, their atypical pyrexia and course, their peculiar cyanosis, their abundant expectoration of almost pure pus—often 10 ounces a day or more—their high mortality and the atypical character of the autopsy findings. Bacteriological investigation carried out by Eyre showed that these cases were examples of a double infection of the respiratory passages—either influenzo-pneumococcal or influenzo-streptococcal. These results were published in the *Lancet*, and agreed in almost every respect with those of similar researches carried out independently in France by Hammond, Rolland and Shore.

Previous to 1917 the cases were for the most part returned under the comprehensive heading of "pneumonia"; but, after they were differentiated from ordinary "pneumonia" and began to be recognized as distinct under the name "purulent bronchitis," cases were returned from nearly every command, with minor epidemics in some, such as Aldershot, and larger outbreaks in others, notably at Oswestry, and amongst the New Zealand troops in the Southern Command in the neighbourhood of Salisbury.

Ætiology.

In 18 out of 20 cases examined in France by Rolland in the winter of 1916, the *Bacillus influenzæ* was found to be present, and in a considerable portion of the cases a pneumococcus was also detected; less frequently a streptococcus, and *Diplococcus catarrhalis* were found in association with Pfeiffer's bacillus. In ten cases the *B. influenzæ* was the predominating organism, and in three no other organism could be seen in the films prepared from the sputum. It seems from these results, and also from similar work of other observers, that the organism most constantly found in the sputum of these cases was the *B. influenzæ*, but that the pneumococcus was frequently also present especially in the cases where Pfeiffer's bacillus was abundant. Pfeiffer's bacillus was constantly present in various infections of the respiratory tract throughout the campaign, and naso-pharyngeal swabs from men who were being examined because they had been in contact with cases of cerebrospinal meningitis, frequently showed its presence in perfectly healthy individuals. It is reasonable to assume that specially debilitating influences of cold and exposure might weaken an individual so that Pfeiffer's bacillus had the opportunity to develop rapidly and, probably in symbiosis with pneumococci or other organisms, to produce this novel picture of acute suppurative bronchitis without broncho-pneumonic extension.

The essential point in connection with the bacteriology of the Aldershot cases was that the infection was shown to be a double one, a combined attack by influenza bacilli and by pneumococci. The influenza bacilli were found mostly early in the malady, the pneumococci prevailed later, and Eyre's conclusion was that the acute beginning and the infectiveness of the disease were both due to influenza bacilli, pneumococci thereafter continuing the attack and causing the purulent bronchitis itself and death from a greater or lesser degree of pneumococcal septicæmia. Practically all the cases in the Aldershot Command that were investigated in this way proved to be influenzo-pneumococcal, but precisely similar cases, especially amongst the New Zealand troops in the Salisbury district, proved on investigation to have a form of streptococcus as the organism associated with the influenza bacillus and not the pneumococcus, so that, whereas the Aldershot cases were influenzo-pneumococcal, other cases were influenzo-streptococcal, and the general impression was that there was no intrinsic reason why yet other organisms might not sometimes be associated with the primary influenza infection in causing the severe purulent bronchitis syndrome. In other words, the bacteriology of purulent bronchitis is not apparently constant. The influenza bacillus seems to be an important factor in its epidemiology, but another micro-organism, associated with the influenza bacillus, plays an important part in the severity of the illness, the combination being in some epidemics influenzo-pneumococcal, in others influenzo-streptococcal, with a presumption that yet other micro-organisms might be found if further epidemics could be investigated.

Morbid Anatomy.

The lungs on post-mortem examination were large and bulky, owing to the presence of much emphysema, but the most characteristic lesion was the presence of thick greenish-yellow pus in all the small bronchi and bronchioles, so that on a section of the lung a large number of greenish-yellow points of varying size were seen scattered over the surface of the section wherever a bronchus was cut across. The pus was thick and completely filled the lumen of the smaller bronchi and bronchioles, so that these were obstructed and contained no air. The mucous membrane of the larger bronchi was congested, and the pus here might be discoloured from admixture with blood. The lung contained many areas of collapse, small in size and scattered in distribution, usually best marked in the lower lobes and towards their posterior borders. No case of massive collapse as a result of purulent bronchitis was observed by Bradford, although some instances of purulent bronchitis were seen as a complication of cases of primary collapse in gunshot wounds of the chest.

Œdema of the lungs, together with much congestion, was frequently present. In at least half the cases that terminated fatally the bronchitic lesions described above were found without any broncho-pneumonia, but in a considerable number of cases small areas of broncho-pneumonia forming nodules, in the centre of which the affected bronchiole could be seen, were also present. Exceptionally these broncho-pneumonic areas were of larger size and by their coalescence considerable areas of consolidation might be produced.

The bronchial glands were frequently enlarged and pinkish in colour, and in some instances the lymphatic glands generally were enlarged. Pleurisy was frequently present but was usually slight, a small amount of lymph being found on the pleura and occasionally a few ounces of clear fluid in the pleural cavity. Empyema was rare. The heart usually showed signs of dilatation especially on the right side, and the muscular substance was pale and soft. The signs of dilatation were most evident in cases where marked cyanosis had been present during life. The kidneys in approximately half the cases showed evidence of change, in that the cortex was pale and swollen and the texture flabby. The renal epithelium was found on microscopic examination to have undergone degenerative changes, and frequently desquamation of the epithelium, much congestion and some round cell infiltration were also present, changes similar to those found in acute nephritis.

The spleen, the liver, and sometimes the kidneys, showed generally signs of engorgement, and fatty changes were not infrequent in the liver.

There was nothing constant about the morbid anatomy of the fatal cases amongst troops in the United Kingdom, except the amount of pus exuding from nearly all the bronchioles when the cut lungs were squeezed. In those cases that had survived a number of days there was generally a considerable amount of diffuse broncho-pneumonia with interstitial hæmorrhage as well; and acute pleurisy, generally without effusion, was frequently present in addition. But amongst the considerable number seen there were several in which, in spite of careful search, no macroscopic evidence could be found of any broncho-pneumonia at all, though the clinical course—beyond perhaps being rather more acute than the remainder—was otherwise similar to those in which broncho-pneumonia was present. In such cases the histological examination of the lung showed remarkable inflammation not only in, but around the smaller bronchioles, a pronounced and extensive bronchitis with peribronchitis, as shown in the following illustration.

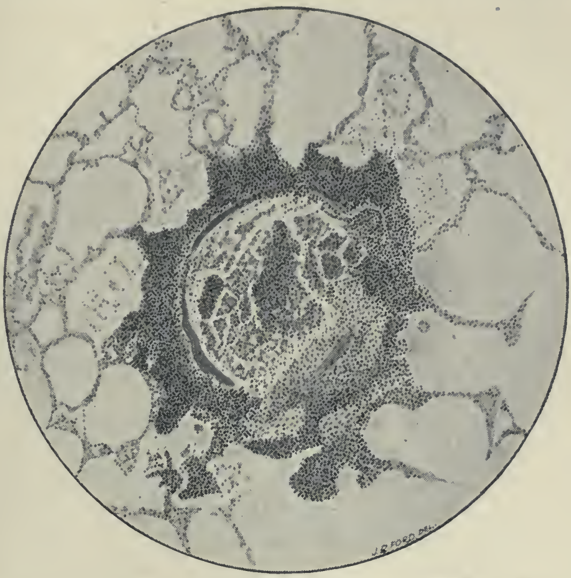

FIG. 1.—Section of lung tissue, under low power of microscope, showing the alveoli to be hardly affected at all, while the bronchiole is filled with cells and débris, and its wall and the immediately surrounding parts are characteristically infiltrated with small round cells.

Symptoms of Cases in France and Flanders.

There was some variety in the clinical picture of the malady in different cases. Some were not only acute in onset, but might be more appropriately described as fulminating, owing to the very rapid development of severe and often fatal lesions. Others were more gradual both in their origin and in their subsequent development.

In the acute type the onset and early symptoms present some analogy to those seen at the onset of acute pneumonia. Thus the onset of illness is sudden and accompanied by high fever, cough and expectoration that may be tinged with blood. Although these symptoms resemble those of pneumonia, there are really certain differences. Thus the pyrexia is not usually as high in purulent bronchitis as in pneumonia, and there is not usually the definite rigor that is characteristic of pneumonia. Local pain in the chest is also not common although there may be much discomfort and sense of oppression. The sputum is not rusty ; if blood is present it occurs as streaks of blood in the sputum, and this rapidly becomes frankly purulent and of a peculiar greenish hue. Cough and oppression are very prominent features, and the dyspnœa soon becomes urgent and is accompanied by cyanosis. This cyanosis develops with great rapidity, and in some of the most severe cases it may take only a few hours for it to become one of the most marked features of the illness. In many cases the patient is of a pale leaden hue, in others the cyanosis is of the usual livid colour. Quite early in the course of the malady the pulse rate is rapid, and quite out of proportion to the pyrexia present. These acute cases may terminate fatally on the fifth day of illness, and in the most severe forms even earlier. Active delirium and excitement such as are seen in pneumonia do not occur; the patient is more apt to be lethargic, although mild delirium may be present.

In the less acute cases the disease runs a very remarkable clinical course. The onset is more gradual, the symptoms of cough and dyspnœa less urgent, although there may be and usually is much fever. The temperature probably reaches 103° F., but it is not sustained and there are daily remissions leading to the production of a chart that presents considerable resemblance to that of a case of tuberculosis or even of enteric fever. In these chronic cases the pulse rarely rises to 120, and it may even be somewhat slow in relation to the temperature. This pyrexia may persist for six or even more weeks, reaching perhaps 102° F., or even 103° F. every day. The pyrexia is accompanied with much sweating and very considerable wasting, so that in many cases there is a resemblance to phthisis, and sometimes it may not be easy to determine apart from sputum examination whether tuberculosis is present or not.

Some cases also have a remittent pyrexia, with two, three, or perhaps more bouts of high fever each lasting several days, separated by intervals of comparatively low temperature.

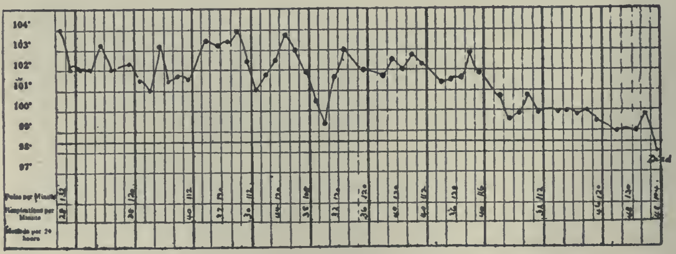

Chart I.—A less acute case, showing the prolonged, rather swinging temperature and the fall by lysis without diminution of pulse-rate just before death. *Bacillus influenzæ* isolated.

The fever may terminate by a critical fall even as late as the third week of illness, more usually it subsides gradually by lysis, but death may nevertheless occur several days after the temperature has reached and remained at the normal level.

The sputum is remarkable in several respects. In the first place it is very abundant. A patient will expectorate from six to ten ounces in less than twenty-four hours, and soon after the onset the sputum consists of nummulated non-aerated masses, each one discrete, roughly the size of a shilling and remaining discrete in the sputum cup. They are of a peculiar greenish or greenish-yellow colour, not offensive, and very occasionally streaked with blood; this is very rare except at the onset and the amount of blood is always small. The character of the sputum and the very large quantities expectorated suggest at first the sputum common in phthisis and in bronchiectasis; but it differs in that it is uniformly homogeneous and purulent, there is no separation into layers, and no expectoration of mucus and muco-catarrhal matter, in fact no liquid expectoration at all, only these nummulated masses. This peculiar sputum is one of the main clinical features of the disease.

Cough is frequent and at the onset painful and distressing; for a short time there may be but little expectoration, and it is at this period that the sputum is apt to contain streaks of blood. When the sputum has assumed its typical purulent and nummular character, the cough, although necessarily very frequent, is often not painful, and the sputum is expelled easily. In the very acute and fulminating cases the cough is often ineffectual, the sputum more scanty, and this is one of the factors in the grave nature of these cases.

The pulse rate is rapid and frequently over 120 even in cases that recover, and, as mentioned above, this tachycardia is one of the main clinical features of the disease. The volume and the tension of the pulse are often good notwithstanding the rapid rate. In severe and unfavourable cases the tachycardia is still more marked.

Dyspnœa and cyanosis are also prominent symptoms; the rate of respiration in all cases except the slightest is considerably increased, and a respiratory rate of 30 to 40 per minute is not unusual when the fever is not higher than 102° F. to 103° F. The dyspnœa causes considerable distress, and in the more severe forms, anxiety; but in the most severe cases where mental dullness or torpor is present, dyspnœa may reach a high degree without apparently causing much discomfort. The cyanosis is very marked and very persistent; it is always a sign of bad omen and the pallid form is the more serious. In the acute and fulminating forms, the cyanosis is most marked and such cases are of the utmost gravity.

The physical signs are usually well marked, although they are not so prominent a feature of the illness as is the case in pneumonia, and the significance of some of the signs, more especially the importance of the presence of areas in which the breath sounds are weak, may be overlooked unless due care is taken. In the earlier stages of the disease, râles and crepitations, fine in character and perhaps rather limited in distribution, are the most marked signs, but together with these the breath sounds are weak and distant, and areas may be found of varying size where they are almost inaudible. The râles are especially fine in character. These signs are most marked in the lower axillary region, and posteriorly between the angle of the scapula and the vertebral column. They may become more or less rapidly generalized, but attention should be especially directed to weakness of the breath sounds, without the presence of any marked impairment of the percussion resonance or any great alteration in the character of the breath sounds. In cases where broncho-pneumonia is also present, the usual tubular breathing and other physical signs of this condition may be made out. The weakness of the breath sounds is doubtless dependent upon the presence of areas of collapse, but these are not generally sufficiently large to cause dullness on percussion, although the resonance may be somewhat diminished. The complete occlusion of the finer bronchioles by the purulent exudate is the probable reason for the absence of tubular breathing over the areas of collapse.

A pleuritic rub in the axillary region may sometimes be heard, but often the presence of pleurisy is not detected clinically owing to the presence of abundant râles masking the pleural friction.

In cases characterized by the presence of cyanotic lividity the usual signs of over-distension of the right heart may be detected, such as epigastric pulsation, fullness and pulsation of the veins of the neck, and increase in the area of cardiac dullness to the right of the sternum.

In many cases, even apart from cyanosis, considerable albuminuria is present and not uncommonly nephritis of a severe type, with not only considerable quantities of albumin in the urine, but also blood. The nephritis, even when severe, is not accompanied by dropsy, but its presence adds greatly to the gravity of the case.

The course of the malady varies; in the acute cases it is measured by days, and in the most severe death may occur on the fifth day, or earlier still in cases of the fulminating type associated with much cyanosis. In the less acute cases the illness lasts many weeks and the high fever may persist for from three to six weeks, or in some cases even longer. In such cases even when recovery ultimately takes place there is great prostration and much wasting.

A remarkable feature of the illness is that death may occur after the subsidence of the fever both in the cases where this occurs by crisis and also where lysis is seen, and the fatal event may not take place until the lapse of two or three days after the return of the temperature to the normal level. Death in these cases is dependent upon one or other of the forms of asphyxia, the result of the blocking of the bronchioles by the purulent exudation.

Symptoms of Cases in the United Kingdom.

The characters of a typical case were briefly as follows. The onset was usually acute, the man falling sick with what he would regard generally as a " feverish cold in the head " and with little about him to suggest that he was suffering from more than acute " coryza " or " febricula." Many such cases would recover quickly and not pass on to the next phase ; some would not even report sick that day at all ; but those cases that were going to be serious—and there was no means of distinguishing these from others—had a temperature of 101° F. or 102° F. the next day, felt ill, began to have a cough and were sent to hospital. The cough was dry at first but within a very short time phlegm began to come up, and by the third or fourth day the sputum attracted particular notice by reason of its large amount. Simultaneously the respiration rate rose to 28, 30, 35, 40, 45 or even 50 to the minute. So rapid and shallow was the breathing in these cases that ordinary lobar pneumonia was at once suspected, and it would have been difficult to persuade those who had not attended post-mortem examinations in such cases that the condition was not really lobar pneumonia. The physical signs found were the same as those found in France and as in France were remarkable for their atypical character. Death might occur without any consolidation at all, and during life the physician was struck by the paucity of abnormal lung signs, although the case was one of obviously severe pulmonary infection. The pulse might be accelerated no more than was to be expected from the temperature—often indeed less so—and the heart's action might remain good almost to the end.

The three most striking clinical features at first were the abundance and character of the pus-expectoration, the relative fewness of physical signs, and the rapidity of the respiration rate. A little later in the disease a fourth point attracted notice, namely a peculiar dusky cyanosis of the face, lips, ears and finger nails, which was always a grave omen. Over half the cases died when once this cyanosis had become obvious. It depended upon the man's natural ruddiness or otherwise what his actual colour became; a sallow man would look dusky-ashen in his forehead, cheeks and nose, but his lips and ears and nails would have the pale bluey-purple hue; whilst a naturally high-coloured man would change from red to a more and more purple or blue-purple hue which might be obvious from the other end of the ward. It was the cyanotic look, not the actual colour, which portended the fatal issue.* The pulse remained good; the cyanosis was not due to heart failure, and it was not benefited by venesection; it seemed to result from anoxæmia, oxygen being unable to gain access to the capillaries by reason of the abundance of purulent secretion in the tubes. Recovery at this stage might occur, but by the time the cyanosis had become at all pronounced the prognosis was extremely bad, although the number of days the patient survived in spite of it was sometimes surprising.

By this time the dyspnœa had often become very marked, respiration consisting of short shallow movements, which in bad cases amounted almost to gasps reminiscent of the effects of gas poisoning. In less severe cases dyspnœa might be in abeyance when the patient lay quite still, yet the slightest effort, such as turning to one side for examination of the back, might send the respiration rate up at once from 30 to 50 or over, this rate not falling to the lower figure again for quite a long while afterwards. The patients were consequently best left undisturbed.

The character of the sputum—pus in abundance—would remain the same for days, though sometimes it would be blood-stained or pure blood might be coughed up independently of the pus. Rusty sputum was exceptional. In the later stages of the illness areas of impaired note or actual dullness might be found, particularly at the bases, associated with bronchial breathing and crepitant râles. These might be due to progression of the purulent bronchitis into hypostatic pneumonia or into actual broncho-pneumonia; or they might be the result of massive collapse secondary to the bronchitis and obstruction of the bronchioles by thick pus; or, again, as the result of pleurisy. This last was not uncommon and not infrequently caused an exudate of a pint or more of thin turbid fluid, which more often than not cleared up after simple aspiration. An actual empyema followed only in exceptional cases.

Defervescence was usually by lysis rather than by crisis, and convalescence slow. Troublesome cough and persistent, though diminished, expectoration might last for weeks, and recrudescence of the mischief, possibly with a fatal termination, after all had seemed to be going well, might occur even several weeks after the primary attack. Many patients, on the contrary, made a complete recovery in a fortnight or three weeks.

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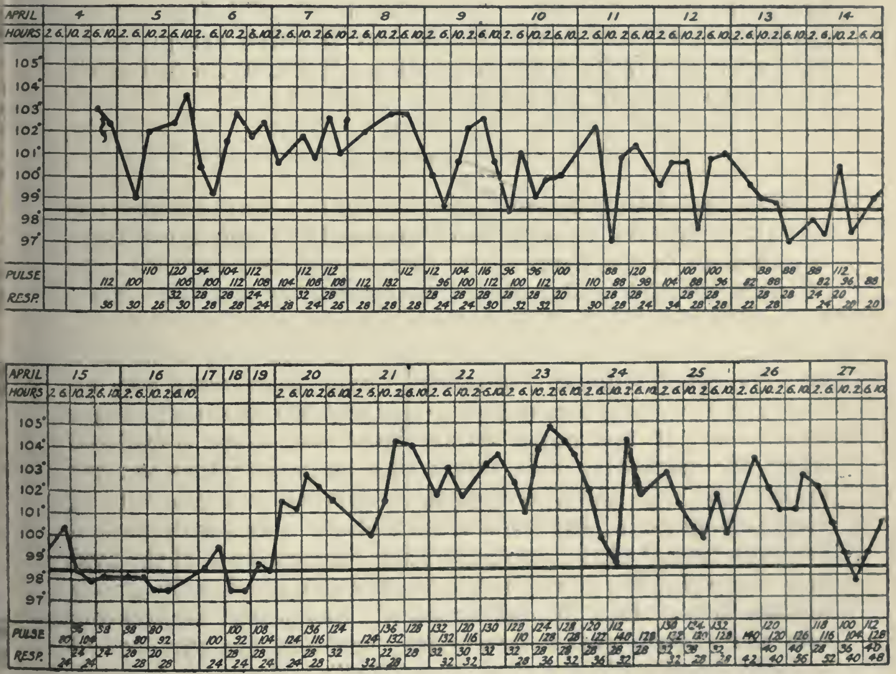
* The plates at page 181 illustrate this condition.

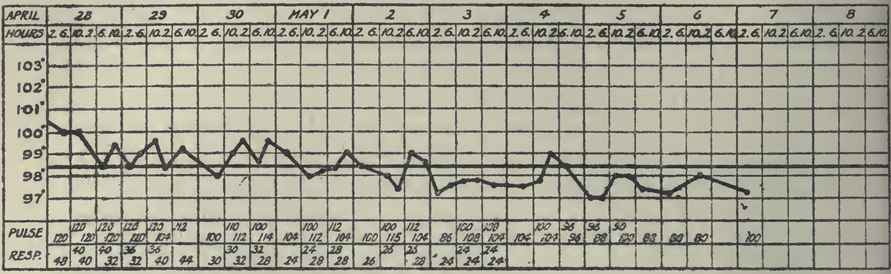
The following chart is typical of the longer cases :—

The patient was a mechanic in the Royal Air Force, age 35 ; service four months. He was admitted to hospital on April 4th, 1917, with a history of having been out of sorts with a cold and bronchial cough for ten days previously. On admission his temperature was 103° F. ; pulse-rate, 112 ; respiration-rate 36. Abundant blood-stained purulent sputum. The accompanying temperature chart indicates the course of the disease. The man was seriously ill with purulent bronchitis for ten days ; improved considerably for a short time ; then relapsed for a week, becoming seriously ill again, but ultimately recovering completely. Throughout the whole time he was in hospital he was coughing up abundant thick yellow pus, which, at first bloodstained, was latterly yellow and free from visible blood. No tubercle bacilli were found. The treatment was mainly by the use of antiseptic inhalations.

The bacteriological findings were as follows. The sputum showed the presence of *B. influenzæ*, *pneumococcus*, and *Micrococcus catarrhalis*.

CHART II.





Complications other than the supervention of broncho-pneumonia or pleural effusion were quite uncommon. The gastro-intestinal tract seemed to escape, except for thick febrile coating of the tongue ; the latter in severe cases was apt to become dry, brown and cracked, from the effects perhaps of rapid breathing through the mouth. This dry cracked tongue was an unfavourable symptom. There was not the same tendency to nephritis that the 1918–19 epidemic of influenzo-pneumonia produced. Mental symptoms—delirium or coma—were not more pronounced than was to be expected in any febrile illness of severity. Sore throats of mild degree were complained of in the early stages, but all other symptoms in the cases were quite overshadowed by the four characteristic phenomena already described.

Prognosis.

With regard to prognosis, the malady is a very serious one and the mortality is very high, especially in the acute type. It is difficult to give figures since these would vary with the type of case included under the term purulent bronchitis. Many cases were seen where the fever was not very high ; the sputum, although purulent and nummulated, was not very abundant, and the general illness was slight. Such cases were not uncommon in wounded men, and frequently subsided with simple treatment. If the more severe cases are alone considered where the symptoms were urgent, the sputum copious and the fever high, it is probable that the mortality was generally as high as 30 per cent. and often much higher. Cases with marked cyanosis did not often recover, and this was true both of the livid and the pallid type, but the prognosis was undoubtedly graver in the latter than in the former. Increasing tachycardia was also a very unfavourable sign, and also the presence of broncho-pneumonia or nephritis. Bodily vigour and youth did not increase the chances of recovery as much as might be expected, and some striking instances were seen where recovery took place in men of relatively poor physique. Age and habits influenced the course of the disease in a manner similar to that seen in pneumonia. In the cases where recovery took place the convalescence was slow and prolonged, but neither relapses nor any permanent ill effects, such as emphysema, were observed by Bradford.

Diagnosis.

The main difficulties in diagnosis are the distinction of the malady from pneumonia in the earlier stages of its progress, and later the liability to confound it with tuberculosis and sometimes with enteric fever. In some instances it may be difficult to distinguish between purulent bronchitis complicated with nephritis and a primary nephritis complicated with broncho-pneumonia. The suddenness of onset and the severity of the respiratory symptoms lead to the confusion with pneumonia, and the long-continued fever of irregular type causes the superficial resemblance to enteric fever and tuberculosis, especially as some cases of enteric fever have not only pulmonary symptoms but sometimes definite pulmonary signs. The abundant sputum and the marked emaciation also are responsible for the confusion with tuberculosis. Examination of the sputum for the bacillus of tubercle will usually enable the differentiation to be made. The essential features in the malady are the remarkable sputum, the pyrexia, the tachycardia, and the cyanosis.

Treatment.

With regard to treatment, it is not surprising, seeing the nature of the lesion in the small bronchioles, that the treatment is not very satisfactory. No line of treatment was discovered which seemed to modify the course of the disease, once it got hold of the patient. The most important point is to try and render the expectoration of the sputum easier to the patient and thus spare his strength. For this purpose a warm moist atmosphere is essential, and a steam tent and hot inhalations are the most serviceable means of securing this. Eucalyptus or Friar's balsam may be added to the hot steam inhalations with benefit. Small doses of potassium or sodium iodide are also useful, and tartar emetic in small doses is also of value in the early acute stage. In cases with livid cyanosis venesection is sometimes beneficial, and from ten to twenty ounces should be withdrawn. Oxygen inhalation is also of use, and care should be taken to warm the oxygen. Although there is much difference of opinion as to the use of digitalis in inflammatory lung disease, it is of considerable value in purulent bronchitis. Adrenalin may also sometimes be given with advantage. Moderately free purgation especially with concentrated saline purgatives should also be employed. No special precautions were taken in France to isolate these cases from other patients in the hospital wards, and during the winters of 1914 and 1916 there was no evidence to suggest that the disease required to be regarded as contagious. The occurrence of many cases in any particular unit or formation at the front showed that under exhausting conditions of cold and wet the disease affected many men, but removal from such conditions was all that seemed necessary to prevent the infection from extending.

In the United Kingdom, however, a different opinion prevailed. In view of the facts that when one case developed in a barrack-room others were apt to follow, and that influenza bacilli were found constantly in the sputum in the earlier cases, the need for the isolation of the earliest cases and disinfection of the abode in which they occurred, in order to prevent the infection spreading to healthy contacts, was strongly emphasized. The question of prophylactic inoculation of troops in a district in which purulent bronchitis has begun to appear has been considered in the chapter on "Influenza." The treatment of patients suffering from influenzal pneumonia is equally applicable to the prophylaxis and treatment of purulent bronchitis.

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CHAPTER IX.

MALARIA.

ÆTIOLOGY, INCIDENCE AND DISTRIBUTION.

OF all diseases responsible for casualties during the war malaria probably holds first place. To realise this fully one has only to look at the figures for admissions for malaria for the three years 1916, 1917 and 1918. In Macedonia they reached the total of about 160,000; in Egypt, about 35,000; in East Africa 107,000 between June 3rd, 1916 and October 27th, 1917; and in Mesopotamia about 20,000. Other places, such as the Cameroons, German South-West Africa, France, and even England itself, contributed to the total, but the numbers are insignificant in comparison with these figures.

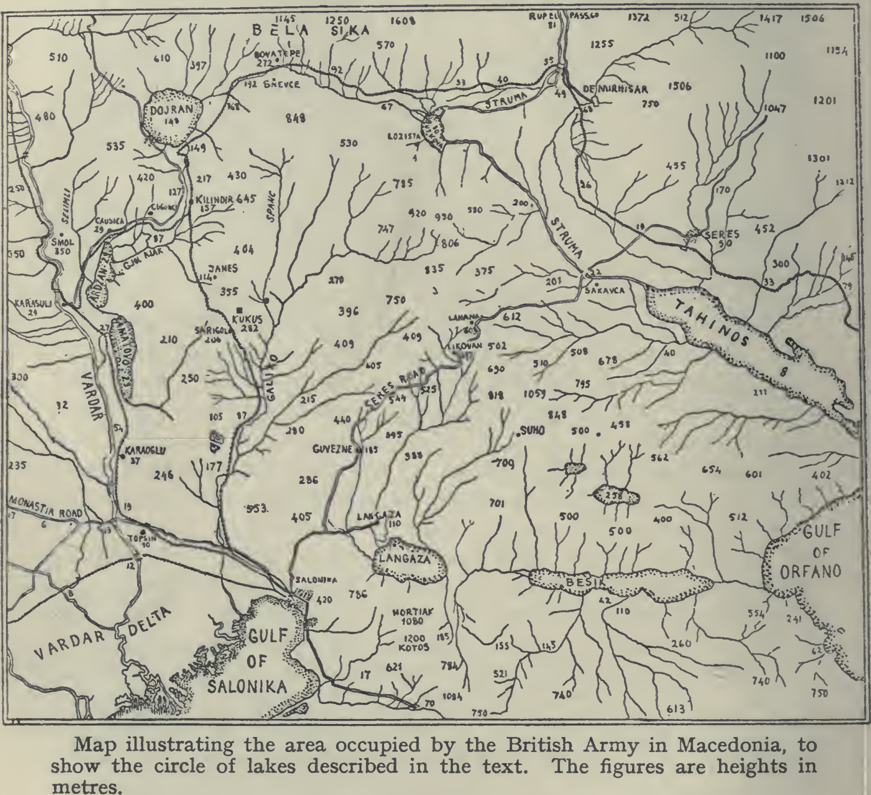
MACEDONIA.

The British Army arrived at Salonika at the end of 1915, after the malaria season was well over. From this point of view a better season could not have been selected, as it gave time for settling down and making a malarial reconnaissance of the country.

Macedonia is a country with a hot summer and cold winter, the extremes being fairly great. The maximum summer temperature in August for the past ten years has been about 90° F., the minimum at the same season being about 70° F. The coldest period is in January and February with a maximum of about 52° F. and a minimum of about 38° F These temperatures are based on the mean daily temperatures, maximum and minimum, for ten years, but they do not represent the actual extremes in various parts of the country. There is a wet season, commencing in the autumn and extending through the winter, and a dry summer which is broken by heavy thunderstorms and great downpours of rain. All these factors are important in that they affect the behaviour of the mosquitoes which carry malaria.

Cardamatis has drawn attention to the fact that malaria is much worse in Greece after a very wet winter and spring, since this condition favours the development of mosquitoes. During the winter much snow falls, especially in the hills, and there are sharp frosts.

The country itself may be described as a continuous series of hills and valleys. In the area occupied by the British there were two large rivers, the Struma and the Vardar, and several lakes. The Struma river with the lakes of Tachinos and Butkova, Lake Doiran, the Vardar river with the lakes of Ardzan and Amatova, and the Lakes Langaza and Besik, form a rough circle in low-lying land. This series of rivers and lakes represents the line which was occupied with such fatal results in the middle of 1916. Surrounding this circle and also within it is elevated country which itself is a complicated system of hills and gullies and innumerable streams. This difference between the low-lying circle and the hilly country corresponded with the distribution of the two chief anopheles responsible for the Macedonian malaria.



Map illustrating the area occupied by the British Army in Macedonia, to show the circle of lakes described in the text. The figures are heights in metres.

The Struma valley with the lakes of Tachinos and Butkova is about 60 miles in length with a breadth of 5 to 10 miles, representing about 400 square miles of fairly flat country. It receives water from all the hills north and south of it and, as in many places it is actually below the level of the Struma, a most intensive breeding ground for mosquitoes is produced.

Marshes occur everywhere, especially about the mouth of the Struma and the two lakes. Many of the streams running down from the hills never reach the main river but are lost in marshes. The Struma valley is very fertile and in spring and early summer presents a glorious picture of green, broken up by acres of wild flowers of every colour and of fruit trees in bloom. As the summer advances the scene is completely changed as on many areas between the marshes the grass is entirely dried up. The valley of the Vardar, with the two lakes beside it, is of a similar nature and consists of low-lying country intersected by streams and broken up by marshes; the same may be said of the Langaza valley.

The hill country, the most important section of which from the British point of view was that within the low-lying circle of lakes, consisted, as already noted, of hills and gullies. In most places there were no trees, but in spring the hills were covered with green, though the grass quickly dried, leaving a brown, burnt-up country. The gullies, however, retained their vegetation of grass, bushes and even trees, because of the countless perennial springs found all over the land. Every gully had in summer its trickle of water, which became a rushing stream or torrent in winter or after the sudden thunderstorms of the hot season of the year. The streams arose in springs at elevations up to three or four thousand feet above sea level. The source was often built in as a fountain by the inhabitants. The overflow would trickle away amongst the stones, flow through stretches of grass or rushes and be completely hidden from view, pass through a rocky channel or disappear in dense brushwood. On every side the stream thus formed was receiving tributaries and increasing in size. Frequently in sandy, permeable soil it would disappear below the ground and be found again lower down the gully. Passing across a stretch of comparatively level ground it would form small marshes or would fall over a ledge into a rocky pool. Eventually reaching the valley it would open into the river or be lost in a marsh. During the summer much of the water dried up and the streams would completely vanish lower down or be represented by isolated pools, but higher up the springs were still present and nearly every gully retained its trickle of water and grass-grown pools.

Hilly country of this nature existed south of Lakes Langaza and Besik and to the east of Salonika, and it was here on the high Hortiak plateau that sites were chosen for summer hospitals.

West of the Vardar river in the area occupied by the French, Serbs and Italians, the country was largely of a hilly nature, though low valley areas also existed. Directly west of Salonika was the delta of the Galiko and Vardar rivers, a large tract of flat country cut up by streams and extensive marshes.

In order properly to comprehend the malaria problem of Macedonia it is necessary therefore to recognize the two types of country, the low-lying marsh, river and lake districts along the circle of lakes and in the Vardar delta, and the high, hilly country around and within the circle.

When the expeditionary force arrived in Salonika the troops were distributed over the hills south of Langaza Lake and about Salonika itself and also on the hills east of the Galiko river as far as Kukus. Troops were also stationed west of Salonika along the Monastir road. The possibility of the occurrence of malaria, especially in this latter area, was recognized, and early in 1916 steps were taken to deal with the area from a mosquito-breeding point of view. At this time it was evident that malaria was to be expected in the marshy country, but the whole system of the countless hill streams proved to be a more prolific source of mosquito production than was anticipated. Had the troops remained in the positions just indicated there would have been undoubtedly a good deal of malaria, but nothing to be compared with what actually occurred after the move forwards in the middle of June, just at the time when the worst malaria season of the year was commencing. Up to the time of the advance there had been about 150 cases of malaria, and of these 90 occurred in June, so that malaria was even then beginning to occur.

At the end of June 1916, the troops moved forwards to the Struma and eventually occupied, in a line running east and west, the whole valley from the mouth of the river to Lake Butkova, thence to the south of Lake Doiran and then over the hills to the Vardar at a point north of Smol. West of this the line was occupied by the French. It was recognized that this was a highly malarial zone from the earliest period of the British occupation; but it was not anticipated that troops would move beyond the perimeter of defences of Salonika, and anti-malarial measures were consequently confined at first to the latter area.

The effects of the advance are clearly shown by the monthly admissions for malaria for one division from June to October inclusive, the successive monthly figures being 4, 1300, 2500, 1600 and 1100. In all there were over 30,000 cases of malaria during the year 1916. From the same line, and behind it in 1917, there were over 70,000 admissions, and in 1918 about 60,000. For the period 1st November, 1915, to 31st October, 1918, the admissions per 1,000 of strength worked out as follows :—

1st November, 1915 to 30th April, 1916 ..	0·24
1st November, 1916 to 30th April, 1917 ..	56·83
1st November, 1917 to 30th April, 1918 ..	162·75
1st May, 1916 to 31st October, 1916 ..	237·28
1st May, 1917 to 31st October, 1917 ..	277·85
1st May, 1918 to 31st October, 1918 ..	253·82

The admissions to hospital which the above figures represent indicate only a part of the incidence, for many cases were treated in field ambulances or in the units without the men being admitted to hospital. Consequently, it is almost impossible to form an accurate estimate of the extent to which the army became infected with malaria. During the influenza epidemic of 1918, 83 per cent. of a series of over 100 autopsies performed by Captain Taylor on men who had died of influenzal broncho-pneumonia showed definite malarial pigment in the spleen without there being active malaria. This figure therefore would probably not be too high an indication of the percentage of the army which actually became infected with malaria in Macedonia.

The anopheline mosquitoes of Macedonia are five in number: *A. maculipennis, A. superpictus, A. bifurcatus, A. sinensis* (*pseudopictus*) and *A. algeriensis*. *A. maculipennis* was universal, but occurred in greatest numbers in the low-lying districts described above. It was the prevalent anopheline of the Struma valley, the Vardar valley, the lakes and the Vardar and Galiko deltas west of Salonika. On the other hand *A. superpictus* was essentially a hill stream mosquito and could be found breeding in any of the streams from their source 3,000 or 4,000 feet above the sea right down to where they broke on to the plains. *A. maculipennis* would be found on the edges of the lakes and in every marsh, however large or small, in the borrow pits, the holes left by horses' hoofs, in tin cans and in fact in any collection of water occurring in the valley. *A. superpictus* bred in the streams, not in the actual current though they could be taken there, but in every little pool or backwater, in the tiny bays behind stones or in the sand, in the small collections of water formed by seepage and in every place where clean and especially alga-growing water appeared. In the streams frogs and water-boatmen abounded and the mosquito larvæ lived with these in perfect harmony. In the lower reaches fish were often present but none of these natural enemies of larvæ seemed able to cope with the intensive mosquito breeding. In the valleys also the same association of mosquito larvæ and their natural enemies was constantly observed. During the summer the whole of the low-lying districts were breeding *A. maculipennis*, and the hill country *A. superpictus*.

A. bifurcatus was not a very important mosquito in Macedonia. Its larvæ could frequently be found in the partially closed receptacles of the built-in fountains in the hills, but it was also found breeding in the streams and in the valleys in small numbers. *A. sinensis* was rarely encountered except in certain localities. It was quite common, however, near the marshy south end of Lake Ardzan and around Butkova. It was taken in other marshy districts, but in small numbers. *A. algeriensis* was taken only once, when its larvæ were collected from a fountain in the hills along the upper part of the Seres road.

Though it has been pointed out that *A. maculipennis* is a valley, and *A. superpictus* a hill mosquito, this demarcation was subject to exceptions. There was a certain amount of overlapping. *A. maculipennis* was sometimes found breeding high up, especially where a stream passed across a comparatively level tract and in its course produced marshes and pools resembling those in the valley, while *A. superpictus* would also be taken in the valley. It must have happened that many larvæ of the latter species were washed down the streams into the valley, especially after the summer thunderstorms. But that the main distribution is correct the following figures will show.

In 1918 Captain Cummins, R.A.M.C., collected during July, August and September at No. 60 General Hospital on the high Hortiak plateau 9,402 anophelines. Of these 9,291 were *A. superpictus* and 111 *A. maculipennis*. Of 2,910 anophelines collected for dissection at Lahanah village 2,000 feet above sea-level, 2,831 were *A. superpictus* and 79 *A. maculipennis*. Of 50 anophelines taken casually at Dragos in the Struma valley in July, August and September 1918, all were *A. maculipennis*. On November 25th, 1918, collections were made at Sakavca in the Struma valley and at Lahanah in the hills. In the former place about 60 *A. maculipennis* were taken in one building, while at the latter the same number of *A. superpictus* was collected. It would be possible to multiply these illustrations, but the above serve to show clearly the relative distribution of the two important Macedonian anopheles.

It is quite clear that the greatest amount of malaria occurred in the valleys where *A. maculipennis* was the chief carrier. Quite apart from any difference that might exist in the carrying power of the two mosquitoes this is what might have been expected. The temperature in the valleys is higher than in the hills, and consequently the mosquito season is longer. In the Struma valley the breeding season extended from May to November, while in the hills it was from July to October. In the valley on warm days in winter mosquitoes would usually attack in the open so that in the valley there was a much longer breeding season. By the time that breeding had commenced in the hills the valley had had a two months' start and was infested with anophelines. These mosquitoes had also been infecting themselves with malaria—in 1916 from the natives and in subsequent years from the troops—so that large numbers of infected mosquitoes existed in the valley by the time that the hill mosquito was beginning to spread the disease. Thus *A. superpictus* in the hills would never be able to overtake either in actual numbers or in intensity of infection the *A. maculipennis* of the valleys. It is for this reason that the greatest amount of malaria originated in the valleys.

It has been suggested that there was possibly a difference in the carrying powers of *A. superpictus* and *A. maculipennis* and that the former, appearing later than the latter, might be especially responsible for the late outbreak of malignant tertian malaria. A similar statement was made in reports on the malaria of Palestine. Wenyon conducted experiments to test these various theories. It was shown that both *A. superpictus* and *A. maculipennis* could very readily be infected with *P. falciparum* and that they become infected to the same extent. With *P. vivax* again both became infected, but *A. maculipennis* a little more readily than *A. superpictus.* It was quite clear that any explanation of the late appearance of malignant tertian malaria, or the more intense malaria of the valleys, which was based on any supposed difference in the infectiveness of the two mosquitoes, was not sound. The mosquitoes appeared to be equally dangerous, but the valleys were the worst places because the mosquitoes were more numerous there and probably more highly infected.

Furthermore, there was no special association of malignant tertian cases with *A. superpictus.* The greatest number came from the valleys, where *A. maculipennis* was the chief vector, but they also occurred in *A. superpictus* areas such as the Hortiak plateau. The same can be said of the severest cerebral types of malignant malaria so that there is no evidence whatever to justify the association of one mosquito with one particular type of malaria. The late appearance of *A. superpictus* and of *P. falciparum* is merely a coincidence dependent on two entirely different factors.

It has been stated that malaria was prevalent to the greatest extent in the valleys, and this is proved by the sudden outbreak which occurred when the troops occupied the Struma valley. All along the front line occupied by the troops and in the more backward area along Lake Ardzan malaria was particularly rife. The very worst places were Karasuli at the south end of Lake Ardzan and Causica at the north end, the south side of Lake Doiran, where two long borrow pits made in the construction of the railway embankment had developed into extensive marshy breeding ground, Dova Tepe, the district about Butkova Lake, and the mouth of the Struma. These places were notoriously dangerous, but the whole front line was very much of this nature, except the short section between Doiran Lake and the Vardar river.

That the hill country, the chief breeding place of *A. superpictus*, was also malarious is well illustrated by the figures for malaria admissions amongst the personnel of some of the hospitals in these situations. The Hortiak plateau, 2,000 feet above the sea, was a beautiful spot which on account of its lower summer temperature was selected as a site for summer tented hospitals. The prevalent mosquito was *A. superpictus* which was found in numbers in all the hospitals in spite of very energetic anti-mosquito work on the streams. There the 61st General Hospital in 1917 had 49 cases of malaria amongst its personnel and 5 amongst the sisters. The 49th General Hospital lost from its personnel each month from June to December, 1, 2, 26, 39, 13, 5, and 2 men respectively from malaria. In August 14 sisters, in September 15, in October 6, and in December 2, went down with the disease.

Here then in an elevated area, where the anopheline was almost entirely *A. superpictus*, malaria was quite common. At the 37th General Hospital stationed at the foot of hills at Vertikop, about 80 kilometres west of Salonika, the malaria incidence was higher. The mosquitoes here were both *A. maculipennis* from the plain and *A. superpictus* from the hills. In 1917 amongst the personnel there were 45 primary cases, and 69 amongst men who had previously had the disease. In 1918 the figures were 55 and 94, giving totals of 114 and 149 for the two years. There were 23 primary and 6 secondary cases amongst the sisters.

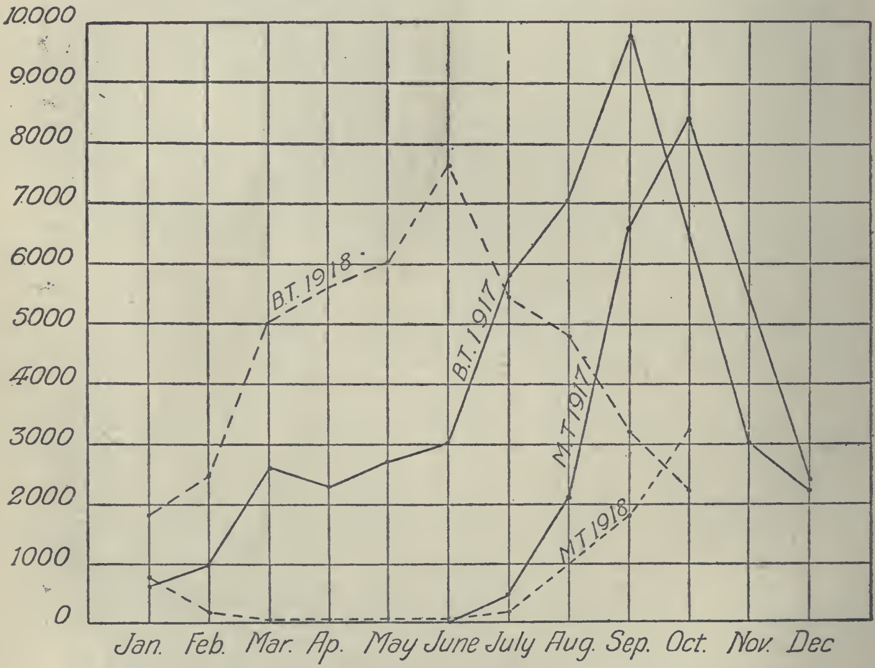
Various theories have been put forward to explain the early appearance of *P. vivax* of benign tertian malaria, and the late appearance of *P. falciparum*. Temperature conditions more favourable to *P. falciparum* in the late summer have been suggested, but experiments show that the difference in temperature required for the development of the two species is really very slight. Roubaud has offered as an explanation the more rapid development of *P. vivax* in mosquitoes. This difference in the rate of development is corroborated by Wenyon's experiments, but is hardly sufficient to account for the difference in the time of appearance of the malaria parasites. A more simple explanation suggests itself. It is well known, and the war has produced much confirmation of this, that benign tertian infections in man are very persistent and relapses are common. An infection, once acquired, tends to persist for several years in spite of treatment. *P. falciparum* infections, though more severe at the time, disappear more rapidly, either as a result of a natural resistance or the greater specificity of quinine for this type of malaria, and an infection rarely tends to carry over into the succeeding year. Thousands of cases of malaria diagnosed as malignant tertian in Macedonia have on return to England and France shown relapses not of malignant tertian, but of a benign tertian infection, which must have co-existed at the time the diagnosis was made. The advocates of the theory which claims that the malarial parasites belong to one species and that the differences merely indicate seasonal or other variations in form have made use of this fact to support their arguments.

In a series of examinations made under the direction of Colonel Dudgeon in Macedonia in the winter of 1916–17, to discover the extent of infection of men in the Struma valley, the following figures resulted. In one series 977 men examined showed 216 *P. vivax* infections, 24 *P. falciparum*, and 1 *P. malariæ*. A second series of 828 gave 222 *P. vivax*, 9 *P. falciparum* and 1 *P. malariæ*, while a third and later series of 1,031 men gave 251 *P. vivax*, no *P. falciparum*, and no *P. malariæ*. Those men were not actually suffering from malaria at the time, but the figures show clearly not only the extent of the carriers amongst the men, but also the tendency for the *P. falciparum* infection to disappear during the winter.

After the commencement of the malaria season each year a large proportion of the benign tertian cases will be relapses or superimposed infections, while the majority of the malignant tertian cases will be definite primary infections. Thus at the commencement of the malaria season there will be a much larger number of carriers of *P. vivax* than of *P. falciparum*, and a larger number of mosquitoes will become infected with the former than with the latter. The first great influx of cases will be benign tertian. Isolated cases of malignant tertian malaria will also occur, and there is a record of an undoubtedly primary case from the Struma valley as early as May.

When once acquired, malignant tertian malaria is more severe and in a shorter time produces a greater number of gametocytes than benign tertian. There will, therefore, be a tendency for malignant tertian to overtake the benign tertian because mosquitoes will more readily become infected in the cases containing the greater number of gametocytes. Furthermore, experiments, mentioned below, have shown some indication that the gametocytes of *P. vivax* are more easily rendered non-infective to mosquitoes by means of quinine than those of *P. falciparum*.

Mention has just been made of the fact that benign tertian malaria occurs earlier in the year than malignant tertian. Very large numbers of blood film examinations were made in the various army laboratories. The tabulated results of about 40,000 positive films for 1917 and 1918 show that towards the end of the year about half the blood films show *Plasmodium vivax* and the other half *P. falciparum*. After this period there is a fall in the proportion of the latter and a rise in the former till, during the period March to



Estimated number of malignant tertian and benign tertian admissions in the Macedonia Expeditionary Force 1917 and 1918. Curve, based on approximately 40,000 positive blood film examinations as collected from the army laboratories by Colonel Dudgeon.

May, when mosquitoes are just becoming active, well over 98 per cent. of the positive films show *P. vivax.* The first influx of fresh cases begins in June to July, and these are mostly benign tertian. The malignant tertian cases do not appear in great numbers till August. If the positive blood film examination of *P. vivax* and *P. falciparum* is taken to represent the proportion of the two types of malaria in all cases admitted to hospital, the monthly admissions for benign tertian and malignant tertian malarias can be estimated. The results are illustrated on the chart on page 236. It will be seen that during the whole year there was a greater number of benign tertian cases, reaching a maximum in August. The malignant tertian cases reached a maximum one month later, but this maximum was lower than that of benign tertian cases. The figures obtained by the armies of the Allies agreed with those of the British. The infection of mosquitoes with malaria of course depends upon the presence of infected individuals. The early incidence of *P. vivax* compared with the late appearance of *P. falciparum* has already been explained as due to the greater number of carriers of *P. vivax* at the early part of the mosquito-breeding season. The mosquitoes which first infected the troops undoubtedly acquired their infection from the native inhabitants, who were largely infected with malaria. When the army advanced to the Struma line the natives were still present in the villages in the valley and the troops became infected from them. The villages were then evacuated, but at the next malaria season so many of the troops were carriers that the native was no longer required as a reservoir for the parasites.

The incidence of malaria depends on two factors: the number of anophelines and the percentage of these infected. There are no figures showing the percentage of infected mosquitoes in the Struma valley. In 1917, 175 anophelines (*A. maculipennis* and *A. sinensis*) collected from hospital tents at Karasuli near Lake Ardzan, a very unhealthy spot, were examined. Not a single infected mosquito was found amongst them. Isolated instances of infection were found amongst anophelines (*A. maculipennis*) collected in the Struma valley, but the numbers dissected were too small to allow of any deductions.

French writers state that in certain localities, especially around hospitals for malaria patients, nearly every mosquito was infected, but such a condition was never found by Wenyon, who consequently doubts the accuracy of the French observations.

Dissections on a large scale were made at Lahanah village, 2,000 feet above the sea. This village was selected because it was accessible, and the natives were known to be highly infected. Thus in October 1917, in films made from eight children *P. falciparum* was found in three, *P. vivax* in one, and *P. malariæ* in one. In June 1918, in films from 52 children attending school, *P. falciparum* was found in five, *P. vivax* in 15, and *P. malariæ* in three, double infections of the two first-named parasites in two and ring forms only in four. Fifty-five per cent. were found infected on a single film examination. In November 1918, a similar result was obtained with 49 per cent. infected.

Lahanah was thus a suitable place to test the infectivity of mosquitoes. In all, 2,831 *A. superpictus* and 79 *A. maculipennis* were dissected through the summer and winter of 1918. The results showed that the highest percentage of infections occurred at the height of the malaria season, for on September 2nd, of 125 *A. superpictus* examined seven were infected, while on August 6th, of seven *A. maculipennis* one was infected.

Taking the figures in four monthly periods the percentages of infected anophelines were as follows :—

November 1917 to February 1918	0·5	per cent.
March 1918 to June 1918 ..	0·3	„
July 1918 to October 1918 ..	1·5	„
November 1918	0·2	„

It was perhaps surprising that in such a heavily infected village a higher infection rate was not obtained. A great deal evidently depends on the opportunity the anopheles have of obtaining infected blood. Thus on September 2nd, 1918, a batch of 42 *A. superpictus* taken from one barn gave six positive results—a percentage of 14. It is highly probable that some infected child had been sleeping in this barn. The result further illustrates the danger of calculating percentages of infected mosquitoes unless large numbers are examined.

In the light of these results it is difficult to understand the high percentage of infected mosquitoes found in Italy at Taranto, which was not nearly so malarious as Lahanah village in Macedonia.

The earliest date on which an infected mosquito was detected was on May 11th, when an *A. maculipennis* taken at Dragos in the Struma valley was found to have oöcysts in the stomach. It is, however, almost certainly the case that infections in the Struma took place much earlier than this.

Macedonia being a country with a hot summer and a cold winter, there is a definite period of hibernation of anopheles. The conditions vary with the elevation and as already explained there is a longer season of mosquito activity in the Struma valley than in the hills. As the cold weather approaches, in October in the hills, and November in the valley, great numbers of large, fat, hibernating females appear and take up their winter quarters. The favourite place of hibernation is in the barns of occupied villages. The Macedonian village house has two storeys, the lower one used as barns or stables and the upper, approached by an outside stair, as a living quarter. The barns and stables are dark, have dirty cobweb-covered beams and rafters and thus make an ideal hibernation retreat for mosquitoes. In those places the anopheles can be found in thousands in the winter—*A. maculipennis* in the valleys and *A. superpictus* in the hills.

On dissection of these mosquitoes during the winter, it was noted that at the early part of the season they were loaded with fat and had immature ovaries; as the season became warmer towards the summer the fat was reduced and the ovaries developed till they were finally mature. Artificial incubation of these mosquitoes during the winter produced the same result. As no hibernating males were found amongst many thousands collected, it was evident that impregnation had taken place before hibernation.

A particular feature of the hibernation was that in many cases it was only partial. In the barns during the winter, cattle, buffaloes and donkeys were frequently housed and these animals acted as veritable stoves, warming up the atmosphere to such an extent that the mosquitoes were rarely completely so moribund as they were in empty barns. A varying percentage of all anophelines collected from such barns was found to contain fresh blood, even on the coldest days, showing that they had taken an opportunity of feeding on the animals. They were indeed seen in the act of doing so. In the Struma valley, and even sometimes in the hills on warm days in the middle of winter, anophelines would sally forth from their hibernation quarters and actually attack man in the open. A number of *A. maculipennis* and *A. sinensis* were taken on the night of March 1st, 1918, in the neighbourhood of Butkova, where they were attacking men very energetically. Of 78 *A. superpictus* taken in Lahanah barns on December 18th, 1917, 14 had blood in the stomach; on January 21st, 1918, of 98 collected 38 had recently fed, and on January 23rd, of 49 fifteen had fed, while on February 9th, of 61 thirty-six had blood in the stomach. The term hibernation as applied to anopheles in Macedonia is thus only relative.

It therefore appears that in Macedonia, at any rate in the warmer valleys, mosquito nets should be used from April to

November, if infection is to be avoided. Even at Lahanah, a mosquito with sporozoites in the salivary glands was taken on 11th November, 1918.

Larvæ of anopheles may survive the winter. This is especially true of *A. bifurcatus*, which bred in the wells. Its larvæ could be found there all through the cold weather, and hatching took place as soon as the conditions became favourable in the spring. In Palestine, further south, this mosquito would pupate and hatch all through the winter, but in Macedonia no evidence of this was obtained.

Larvæ of *A. maculipennis* were found to withstand freezing. They could be frozen in a solid block of ice for 24 hours or more and be still living when the ice was melted, but though possibly this mosquito and *A. superpictus* might thus be able to survive the winter in the larval state, the hibernation of the adult female is undoubtedly the method by which these mosquitoes tide over the cold weather. No observations were made on the hibernation of *A. sinensis* though, as already stated, it was found biting in the open at Butkova as early as 1st March.

The series of dissections carried out at Lahanah of hibernating mosquitoes revealed an interesting fact. All through the cold weather mosquitoes with partially developed pre-sporozoite cysts were discovered. These cysts had a perfectly normal appearance and the question at once arose as to whether it would be possible for such cysts to continue their development if temperature conditions became more favourable.

A series of experiments was instituted to test this point. Batches of mosquitoes were fed on crescent cases and incubated for about a week. Some of the mosquitoes were dissected and the size and condition of the cysts noted. The remaining anopheles were then exposed to the ordinary indoor winter temperature (9·6° C.—18·2° C.). By dissecting specimens at intervals it was noted that the cysts had remained without further degeneration. After three weeks a further incubation was found to bring about complete development of the cysts. It was thus demonstrated that development could be completely arrested and then continued, so that carriage of malaria through the winter by mosquitoes themselves becomes a possibility. Before finally deciding the point, however, it will be necessary to discover if development could be arrested for longer periods, such as three months.

When after such partial development mosquitoes were placed in the ice chest (9° C.—12° C.) for a week it was found that degeneration of the cysts took place, as evidenced by shrinking of the contents and crinkling of the cysts. Exposure to a temperature of 5·5° C. in the ice chest for a period of

12 hours did not cause any degeneration. It thus appears that in nature a short exposure to cold, as, for example, a very cold night, would not cause the cysts to degenerate.

A difference between *P. vivax* and *P. falciparum* seemed to occur in respect of the effects of quinine on the gametocytes. In one *A. maculipennis* and 12 *A. superpictus* fed throughout the experiment on cases infected with *P. vivax* taking quinine there were no infections, while of five *A. maculipennis* and 15 *A. superpictus* fed at least once on a case not taking quinine there were eight infections.

With *P. falciparum,* however, of 40 *A. maculipennis* and 37 *A. superpictus* fed on cases taking quinine 30 of the former and 26 of the latter were infected. It appeared that the quinine had a greater effect on the gametocytes of *P. vivax* than on those of *P. falciparum* in rendering them non-infective to the mosquitoes.

The experiments are not conclusive, for it generally happens that the *P. falciparum* cases selected for experiment harbour more gametocytes than the *P. vivax* cases. In fact, *P. falciparum* as a general rule develops gametocytes in greater numbers than *P. vivax.*

If this action of quinine is a fact then it seems that a regular administration of quinine during the winter to an infected population would do more to rid it of *P. vivax* than of *P. falciparum.* On the other hand, *P. falciparum* infections respond to quinine more readily than those of *P. vivax.*

Many statements have been made as to the peculiar severity of the malaria in Macedonia, and some have even sought to discover some special feature in the malaria parasites themselves to account for this. It is true that in 1916 the mortality was fairly high for malaria (1·01 per cent.), but it must not be forgotten that the great outbreak came as suddenly and unexpectedly as a Macedonian summer thunderstorm, and that the arrangements for dealing with such a large number of sick were at first inadequate. The roads along which the patients were brought to the base were at the time in a very bad condition, and it is only surprising that the mortality was not greater. In 1917 and 1918, with greatly improved conditions of transport and treatment, the most important of which was the wonderfully constructed Seres road, the mortality was much lower (·37 and ·31 per cent.), though the malaria to which the troops were exposed was the same. The number of cerebral cases of malaria was not really great when compared with the large number of *P. falciparum* infections. It seems extremely improbable that the proportion of serious cases was any higher in Macedonia during 1917 and 1918 than amongst any group of individuals living in any other area where malignant tertian malaria occurs. The feature of the malaria of Macedonia, therefore, which made it so serious was the very large number of cases and not the greater proportion of severe cases amongst them. They were numerous, of course, but only because the total number of cases was so overwhelmingly great.

The hardships of war added to the severity, but even these did not produce as high a mortality rate as frequently occurs on a much smaller scale in other parts of the world.

It was frequently noted that any sudden change in the habits of the troops which necessitated great expenditure of energy or exposure to hardship caused the malaria infection of many to become active, though before this they had established some sort of balance between the parasites and themselves. Sudden exertion or exposure broke down this balance and relapses occurred.

A careful examination of the malaria parasites themselves did not reveal any peculiarities. They were identical in every way with those which had previously been studied in other countries. The intensity of the infections in the severe cerebral cases, with the capillaries of the brain and other organs blocked with infected cells, and the enormous numbers of parasites sometimes seen in smears of the spleen, have been noted on many occasions in cases dying of cerebral malaria in other countries.

Macedonia is probably the worst malaria country in Europe, but there are many parts of the world equally bad, which would have produced the same disastrous results if an army of susceptible individuals like that of the expeditionary force in Macedonia had been campaigning there.

Natives undoubtedly formed the original reservoir from which the troops acquired malaria in 1916, but, as already stated, in subsequent malaria seasons the troops were infected to such an extent that they formed their own sources of infection for the mosquitoes. Among the troops *P. vivax* and *P. falciparum* were the common forms of the malaria parasite. *P. malariæ* was so rare as to be a curiosity. It was at first thought that the isolated cases of this infection were in men who had probably acquired it in some other country, but this was afterwards found not to be the case.

The malaria rate amongst the natives was very high and spleen indices taken amongst the children gave figures varying from two to nearly 100 according to locality. Blood films taken from children in Lahanah village gave a high percentage of infections, as already noted. After the armistice a series of films was made from children in villages in the valley of the Strumica, a river in Bulgaria flowing into the Struma just north of the Rupel Pass. The percentage of infections for six villages varied from 11 to 52, and as only a single film was examined in each case it is evident that the infections must have been very high in some of them.

An interesting point in connexion with the examinations of the native children was the frequency of *Plasmodium malariæ.* In one village in the Strumica valley nineteen films gave eleven positive results, and six of these showed the parasite of quartan malaria. This is all the more remarkable when the rarity of this particular parasite amongst the British cases is remembered. Two experiments to infect anopheles with *P. malariæ* failed to produce any positive result.

In 1916 anti-mosquito measures were commenced in the area west of Salonika along the Monastir road. In 1917 the work was greatly extended and included practically the whole of the area occupied by the British. In 1918 more still was done with gangs of native labour added to those of the troops and every known device for combating the breeding of mosquitoes was in practice. The extent of the work carried out in 1918 was enormous and it is difficult to see how more could have been done under the actual conditions. The area involved was many hundred square miles of country, all of it, whether on account of the streams on the hills or the marshes in the valleys, affording facilities for mosquito breeding. The troops were scattered over the country and in very many cases it was only possible to deal with a limited area round each camp. Beyond the area, usually a half-mile limit, breeding still continued, and much of the work was wasted because of mosquitoes which travelled in from without.

The range of flight of the mosquito, especially when it can be done in stages, is not half a mile but often two or three miles or even more. The absence of a population near a breeding ground encourages the mosquito to travel long distances to find a host upon whom it can feed. The result is that the camps, though surrounded by a cleared area of half a mile, even if this area was properly maintained, became the centre of attraction for mosquitoes breeding all over the country. In the valleys the conditions were worse than in the hills, for so much breeding ground existed immediately beyond the British lines that the partial treatment of what was within it was of little avail.

In dealing with the hill streams two difficulties had to be encountered. During the summer the streams were constantly shrinking and many of them actually dried up, but in process of so doing the conditions were constantly changing so that new pools and breeding places were continually forming. A careful watch had to be kept and the stream could be controlled only by weekly inspections. The second difficulty was the occurrence of the summer thunderstorms which would in a few minutes convert a tiny trickle into a roaring torrent capable of washing away men or animals. The work of weeks would in this way be destroyed in a few minutes.

If anti-mosquito measures are a complete success the anopheles will disappear from the area. If they are still present it proves either that the work is not sufficient, not properly carried out, or that it does not extend far enough.

Many statements were made about the diminution in mosquito density as a result of the measures adopted, but there are no actual figures of mosquito density for several years wherewith results can be controlled. However, observations were made in areas where a great amount of anti-mosquito work was done. On the Hortiak plateau, for example, during the two months 23rd July to 24th September, 1918, over 9,000 anopheles were collected from the hospital marquees of No. 60 General Hospital. These mosquitoes can only have been a small percentage of those actually in and about the camp. The other hospitals on the plateau were similarly situated. Consequently, in spite of the energetic measures, the area was heavily infested with anopheles. Unless therefore the mosquitoes could have been reduced to a very much greater extent than was the case, little hope of reducing the malaria could have been entertained. For when the mosquitoes are very numerous a reduction by 50 per cent. does not mean a 50 per cent. reduction in the chances of infection, as it matters little whether a man is attacked by 10 or 5 infected anopheles. In either case the chances of infection are practically certain.

In another area, Guvezne, where energetic measures were carried out, a similar state of affairs existed. The tents of a casualty clearing station there in September were simply swarming with *A. superpictus* and half an hour's collection by two people yielded several hundred mosquitoes.

Near Lahanah a casualty clearing station moved out one day and its site was occupied by a field ambulance the next. Very careful work had been carried out in all the streams for a half-mile radius, yet the first morning after the field ambulance marquees had been erected over 700 anopheles were taken from 7 marquees.

Similar conditions existed everywhere though it was frequently reported that no mosquitoes were present. The discovery of anopheles in tents and buildings is not so simple a matter as many imagine. A mere glance round might reveal nothing, yet on careful search under flaps and in corners or amongst hanging clothes anopheles would be found hiding. These insects disappear during the day into any dark retreat and it is for this reason that erroneous impressions of their absence constantly arose. Powers of observation also vary considerably amongst individuals, for in rooms with mosquitoes actually flying about the windows at the time some observers have failed to notice them. Impressions as to their presence or absence or their relative numbers have therefore often been found to be of no value whatever, even when the information has been given by those who might have been expected to know something of the habits of mosquitoes.

For these reasons it is very difficult to estimate the value of the anti-mosquito measures in Macedonia. The area was so vast that it was an impossible task to exterminate the mosquito in a short time, and probably no one imagined that more than a partial success could be attained. It is questionable therefore whether the measures employed reduced the mosquito incidence to such an extent as to justify the amount of labour expended. In the areas mentioned above it would seem that this was not the case, and yet these areas were comparatively easy to deal with when contrasted with the extensive valley regions of the Struma and Vardar. In certain districts such as the plains about Janes, in the hill section of the front line between Lake Doiran and the Vardar and possibly in the Dudular area west of Salonika on the Monastir road, some good may have resulted, but in most places the mosquito incidence was still so high that infections can have been only very slightly reduced.

In 1918 a light form of mosquito-proof hut, consisting of wood, canvas and gauze, was put up on a large scale even near the front line. In these huts the men had their meals or sat in the evenings before retiring for the night. It is reasonable to suppose that, if it had been possible to supply every unit with a sufficient number of these huts before the malaria season started, a very appreciable degree of protection would have resulted.

A very satisfactory type of bivouac mosquito net was designed in 1918 as the result of previous experiences. The faults were that there was only one net for two men and that there were not enough nets to enable damaged ones to be replaced at once. A net for each man with a sufficient number in store in each unit for immediate replacement of damaged nets would have been an advantage.

There were many other protective measures and they all had their uses, but it would seem that a properly carried out campaign of protection against the mosquito would have reduced the incidence of malaria more than the unavoidably imperfect and partial anti-larval work carried out in Macedonia.

ARMY OF THE BLACK SEA.

After the armistice the British Expeditionary Force in Macedonia moved eastward where it became the Army of the Black Sea and occupied various positions around Constantinople, the Black Sea, the Caucasus and as far as the Trans-Caspian regions.

Naturally many relapses occurred amongst the former Macedonian troops but most of the cases were sent to England as soon as possible. The improvement in the general condition, however, was very marked, there being only 7,480 cases of malaria for the whole of 1919.

Constantinople itself was a veritable health resort after Macedonia. There was practically no malaria in the town and very little round about. *A. maculipennis* was prevalent in the valley of the " Sweet Waters of Europe " but very little primary malaria resulted. In the hills north and west of Constantinople there appears to have been some primary malaria due to *A. superpictus*, and again on the Asiatic side along the Baghdad railway some cases of primary malaria occurred, probably due to the same mosquito. At a small port on the Asiatic side of the Bosphorus near the Black Sea a small outbreak of benign tertian malaria occurred amongst the troops holding a fort.

Batoum, at the Black Sea end of the Trans-Caucasian railway, was highly malarious. The town itself was on a level stretch of land surrounded by hills. There was a heavy rainfall, the driest month of the year being reputed to yield three inches. The result was that vegetation was abundant and there were endless facilities for mosquito breeding. *A. maculipennis* was the commonest mosquito breeding in the marshes and pools. *A. superpictus* was rarely taken in the hills behind. The malaria was undoubtedly due to the *A. maculipennis* breeding about the town.

The railway from Batoum to Baku ran through .highly malarious country. Tiflis itself was practically free though the surrounding country was heavily infested with anopheles, especially along the Tiflis-Baku section of the line. At practically every station high towers had been erected so that the station staff could sleep at nights above the low-flying mosquitoes.

The need of these was evident, for an examination of the station buildings, especially the latrines, showed them to be heavily infested with *A. maculipennis*. In one latrine many hundreds of these mosquitoes were found sheltering from the light of day. *A. sinensis* also occurred but was seen in much smaller numbers, while the miles of plain through which the railway passed were teeming with the ferocious *Ochlerotatus dorsalis* (*O. caspius*) which boarded the trains even when in motion and attacked the passengers with intense voracity.

An experience of 305 N.C.O.'s and men of the Royal Warwickshire Regiment who were sent to a post south of this line is of interest. They chose as a camp a site on the banks of a small stream at Varda. In a fortnight's time cases of malaria occurred and, as these increased in number, the whole unit was quickly removed to a healthy site on the hills above Tiflis. Here practically every man who had not already malaria quickly succumbed. In all, 303 of the 305 were known to have gone down with the disease. This is a good illustration of what may happen when exposure takes place without any protection. Prophylactic quinine was not taken, nor, it is believed, were nets used, and the sick rate from malaria in the few weeks the troops were stationed at this spot was practically 100 per cent.—a rate which was considerably higher than in any of the worst spots in Macedonia, where prophylactic quinine may still have protected some individuals from infection or prevented relapses though it failed to protect the majority.*

Another highly malarious spot was Petrovsk on the Caspian Sea, the headquarters of the Royal Flying Corps. Here *A. maculipennis* abounded and many cases of malaria, both malignant tertian and benign tertian, occurred.

The whole of the plains in this country are highly malarious, but the hills are relatively free and, as it was possible to select the sites for camps during the British occupation, unnecessary exposure did not take place, except in the case of incidents such as that noted above. The malaria situation had been considered by the Russian Government and schemes of improving the country had been drawn up before the war. Literature in Russian had been published, maps constructed and leaflets and placards for propaganda purposes prepared. The outbreak of war, however, had frustrated these schemes.

PALESTINE AND EGYPT.

Malaria became of great importance after the active operations in Palestine had commenced in 1917–18. In 1916 there were scarcely more than 1,000 cases reported from Egypt. In 1917, during the latter part of which the operations against Palestine had commenced, there were 8,480 cases, while in 1918 there were over 28,000. In 1919, after the operations were over the number fell to about 6,400.

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* Wenyon states that on several occasions when prophylactic quinine was stopped the incidence of malaria immediately increased.

The malaria of 1916 occurred chiefly in the Canal Zone, the Fayoum (Senussi campaign), and the Western Oasis (Dakkla). In the Canal Zone the most abundant anopheles were *Cellia pharoensis*, the commonest anopheline of northern Egypt, *A. turkhudi*, and *A. mauritianus*. Both the former were shown by Manson-Bahr to be carriers of malaria. In the Fayoum *Cellia pharoensis* was the carrier.

In the Western Oasis an outbreak of malaria occurred ten days after the arrival of troops at the end of December, 1916. In this instance the vector appears to have been *A. turkhudi*.

The expedition against Gaza in 1917 did not produce much malaria, but after the successful operations of November, 1917, and the movement forward of the troops, it was evident that a highly malarious country had been occupied and the conditions were completely changed. The line occupied by the troops at the end of 1917 consisted of three distinct sectors : the seaboard line from a point a little north of Jaffa to the hills, the line over the hills in the direction of Jericho, and the Jordan valley line north of the Dead Sea. As regards the mosquitoes and the malaria incidence these three sectors differed considerably.

The temperature conditions in the three sectors were not the same. The mean daily temperatures were highest in July and August, being just over 78° F. at Bir Salem in the coastal plain with a minimum of about 67° F. At Jerusalem the corresponding temperatures were 73° and 61° F. and in the Jordan valley 87° and 75° F. It will be evident therefore that the temperature of the coastal sector was 5 to 6 degrees higher than at Jerusalem, while in the Jordan valley it was higher than on the coastal plain. If 60° F. is taken as the temperature below which mosquitoes will not breed, then in the Jordan valley they would have commenced in March, on the coastal plain in April and in the hills in May, It will be seen that this was a little earlier than in Macedonia, as was to be expected in a country so much further south.

The British line crossed the coastal plain, the hills and the Jordan valley roughly at right angles and in this respect it differed from the line in Salonika which ran along the whole length of the Struma valley from the sea to Lake Butkova. The Palestine line was roughly 60 miles in length with 10 miles of this on the coastal plain, about 40 on the hills and 10 in the Jordan valley. As the hills were relatively free from malaria it is thus apparent that the exposure to infection, other things being equal, was much less than in Salonika.

The coastal area consisted of sand dunes parallel to the sea and within them a marshy plain, through which ran the river Auja with its numerous tributaries. On the eastern side were the hills, down the valleys of which streams ran to the plain. The hill country did not, however, have the very extensive stream system found in Macedonia and in consequence anopheles were very much less numerous. Furthermore, the drying up of these streams during the summer was greater than in Macedonia and there was not the same danger from sudden thunderstorms. In the Jordan valley there were the river itself and its tributaries with marshes along their course and hill streams running into the valley.

A feature of Palestine was the system of wells. These were found everywhere, especially in the villages of both the coastal plain area and the hills, and they were taken advantage of by the anophelines to a much greater extent than in Macedonia, where the wells and built-in fountains in the hills were not such sources of danger as the streams themselves. The worst areas from the malaria point of view were the two marshes, the Burak Leil about half-a-mile long by some 200 yards broad, and the Baharet Katurieh about one mile long and a third of a mile broad, in the coastal plain. In addition, in this area was the river Auja from its source near the foot hills to the sea. It had numerous tributaries and one of these formed another marsh, the Tel Abu Zeitun. The two main marshes, however, had been drained and anti-mosquito measures had been taken along the greater part of the river system.

There was therefore in this sector nothing comparable to the Struma valley with its large lakes and extensive marshes, such as those surrounding Lakes Tachinos and Butkova, which were breeding millions of mosquitoes. The river Auja presented greater difficulties but the length to be dealt with, including its tributaries and marshes, was short compared with the river Struma and its tributaries. The Auja river was attacked with great energy and most of the water-ways cleared, so that in this sector practically all the breeding places up to the outpost lines were under control. The wells also were rendered harmless by regular oiling.

Here then was an area which, though it involved a great expenditure of labour, held out some prospect of success in the prevention of mosquitoes. There was, however, this drawback, that no anti-mosquito work was done on the enemy's front, and consequently there was always danger of invasion by mosquitoes from that quarter. It is probable that invasion of this kind took place but perhaps not to a great extent, for the mosquitoes would probably find sufficient attraction in the Turkish army to prevent them wandering far afield; but in some cases oiling of pools was carried out right up to the Turkish wire.

In the Judæan hill sector there were the streams and the wells. The streams ran on the one hand to the coastal plain and on the other into the Jordan valley. The hills and gullies of Palestine were, however, much drier than those of Macedonia. A far greater number dried up completely in the summer so that, though some of them were perennial, their limited number made it possible to clear them. The real danger in the hills came from the wells, but as every one of these could be discovered and recorded they could be rendered innocuous by systematic oiling.

In the Jordan valley conditions again changed; there were wells to be dealt with and again the river system with its consequent marshes. The line was a short one, barely 10 miles in length. It was the worst sector and the most difficult to control. There were extensive breeding grounds at Musallabah and other places beyond the British lines, and every night, helped by the prevailing wind, mosquitoes invaded the lines and caused a very high incidence of malaria. The conditions in the Jordan valley may be said to have resembled those of the Struma valley.

The important malarial mosquitoes were *A. bifurcatus*, *A. superpictus* (*palestinensis*) and *A. maculipennis*. The first was the well mosquito. Its larvæ and pupæ occurred in wells all through the winter and hatching took place on warm days. This was true not only of the wells in the valleys but also of those in the hills. In Macedonia this mosquito was not of great importance, though there also its chief breeding place was the wells. There also the larvæ survived the winter but the more rigorous winter climate of Macedonia rendered them less active than in Palestine. *A. maculipennis* was the common mosquito of the coastal area and along the Jordan valley. Its breeding habits in the marshes were the same as in Macedonia. *A. superpictus* was also observed in the valleys but it was chiefly found breeding in the clear water near springs and in rivulets. It was also the mosquito of the streams in the Judæan hills; so that, as in Macedonia, *A. superpictus* may be said to be the hill stream mosquito and *A. maculipennis* the mosquito of the valley.

Another mosquito was the *A. sinensis* (*pseudopictus*), which was found in marshes and sluggish water in the coastal sector, and had habits similar to those of the same species found in Macedonia.

A mosquito not occurring in Macedonia but seen in Palestine was *A. turkhudi,* which was found in some of the rivers of the Jordan valley. *A. algeriensis* was also observed occasionally.

As regards the incidence of malaria an attempt was made to estimate the number of primary cases amongst the three corps holding the front line. Altogether some 8,500 primary cases occurred between April 1st and October 1st, 1918. This gives a ratio of just over 5 per cent. of the strength. The rate was highest, about 8 per cent., in the Desert Mounted corps in the Jordan Valley. It was 6 or 7 per cent. in the 21st Corps in the coastal region and only 1 per cent. in the 20th Corps holding the hill area. This is what might have been expected from the mosquito distribution in the three sectors.

The 7th Division, occupying a position near the Baharet Katurieh, had a high incidence of malaria. From June to September the cases of primary malaria were 2,060, or 11·4 per cent. of the average strength. They were exposed to *A. maculipennis,* many of which are stated to have come from the Turkish lines. The 3rd and 54th Divisions occupied the Auja river area. Amongst them 1,800 cases of malaria occurred, or 10 per cent. of the average strength.

In the Jordan valley the Desert Mounted Corps changed very much in composition during the summer but the incidence curve of malaria showed a steady rise from May with a maximum in July. There then followed a fall, which was attributed to the anti-malaria measures. In other words, it was thought that the reduction in the number of mosquitos was causing fewer infections. Yet a rise in the curve from 7th to 10th August and on 7th September was explained by the fact that new units joined the corps and within the first two or three weeks of their stay in the valley had a large number of cases. This incident was against the supposition that the anti-mosquito measures had been responsible for the fall in malaria amongst the non-infected men already there. It must be remembered, however, that the incidence rate of malaria is highest at the commencement of the occupation of a malarial area and gradually diminishes, quite apart from any reduced exposure to infection. Amongst a large body of new arrivals the initial malaria rate will gradually fall, owing either to the weeding out of the most susceptible, to an acquired immunity, or to the establishment of a balance between the host and the parasite.

Very instructive curves of the incidence of benign tertian and malignant tertian malaria have been made from the results of the laboratory diagnosis of the coastal and Jordan valley sectors. In the Jordan area there was a rise in the number of benign tertian films from May to a maximum at the middle of June. There was then a fairly steady fall to the end of the year. The malignant tertian cases rose more slowly and more irregularly to a lower maximum in the second week in August. There was then a fall for one week, a rise to a point a little lower than the maximum the next, and then a still greater fall followed by a steady rise during the latter part of August and September.

The final advance of the British in Palestine commenced on 21st September, 1918, when the troops went forward over the old Turkish lines, but any increase in infections resulting from an advance into untreated mosquito-breeding country would not be evident for at least a fortnight later, so that the rise in malignant tertian incidence up to 5th October may be taken as due to infections acquired while the troops were still in the original area. It is necessary to deal with this aspect of the question for there is a tendency in reports to assume that up to the time of the advance there had been a steady fall in the malaria rate, and that, but for the advance into untreated areas, the malaria rate would have continued to fall. In the Jordan valley area at any rate there was evidence that the malignant tertian outbreak which would be expected in the autumn had just commenced before the advance, and was running concurrently with it. During the advance, however, the figures undoubtedly rose considerably higher than they would have done if the troops had remained stationary in their original lines. This was probably due both to the increased hardships associated with the advance and to the impossibility of employing the methods of protection to which the troops had become accustomed while they were stationary. It is not suggested that the anti-breeding measures carried out in the Jordan valley were not responsible for a reduction in the malaria, but that in spite of these, and in spite of the protection given by nets and other means, there would still have been an autumn rise in malignant tertian malaria. In this case the curves would correspond closely with those of Macedonia where the benign tertian infections began to fall while the malignant tertian infections rose to their maximum in October. In Macedonia the troops were stationary and the incidence could be observed without the complications of a sudden advance.

The corresponding curve of the coastal area, however, appears to illustrate the effect of the advance more conclusively, for there was a definite and striking rise in the malignant tertian rate exactly a fortnight after the advance commenced. There was a similar but less marked benign tertian rise which commenced a week later. Here then there seems more reason for assuming that the rise was due to the advance, but it is impossible to state that no rise would have taken place even if the troops had remained stationary. In a report on malaria conditions in Palestine, Syria and Cilicia in September 1919, by Lieut.-Colonels E. C. Hodgson and R .C. Watts, I.M.S., and Lieut. P. Barraud, a curve showing the incidence of primary malaria in 1919 is given. It shows the usual marked rise in malaria in September and October and is the kind of curve which would probably have resulted if no advance had originally taken place and the troops had remained in the Jaffa-Jericho line through the autumn of 1918. This curve conforms very closely with the incidence of malaria in Macedonia.

In Palestine no systematic collection of mosquitoes on a large scale was undertaken, and only a few accurate scientific observations of their habits are recorded. These refer specially to the presence of mosquito larvæ.

In 1919 the relative incidence of malaria in the areas occupied by the British, taking the incidence in Cilicia, the worst district, as 100, is as follows :—

Cilicia	100
Syria (not including Lebanon)	31·0
Palestine	23·0
Suez Canal Area	3·6
Egypt	2·6

Observations were made in Palestine on the temperature conditions favouring the development of mosquitoes. It was found that eggs of anopheles have seldom been laid in a season when the temperature exceeded 70° F., while a temperature below 60° F. retarded their development. A temperature between these levels was the optimum not only for the laying, but also for the hatching of the eggs and the further development of the larvæ. It was further noted that the adult anopheline is a moist insect and in consequence of evaporation through its tracheal system its temperature is not necessarily that of the surrounding air. Differences in the relative humidity of the atmosphere had marked effects on the adult mosquitoes. In a dry atmosphere, provided there is food and water, the mosquito will tolerate a high temperature, whereas a humid atmosphere is unfavourable.

EAST AFRICA.

Whereas the conditions favouring the spread of malaria in Macedonia and Palestine closely resemble one another except that in the latter the temperature is higher and the extent of summer drying of the hill streams greater, in the East Africa campaign very different conditions existed, and another group of anophelines came into play. In the earlier period of the campaign there was a considerable amount of malaria, but the greatest incidence occurred after Dar-es-Salaam became the base. Although the problem of dealing with malaria presented itself in connection with the occupation of other coastal towns and up country, where, however, little could be done beyond the use of protective measures against the bites of mosquitoes, Dar-es-Salaam was probably the most malarious locality within the area of operations and the danger of its incidence existed throughout the whole year. The town lay to the north of an inlet from the sea and into it ran the Gerasini Creek, where the most extensive mosquito breeding grounds existed. Breeding grounds also existed in the town itself and north of it ; in fact the whole area was dotted over with marshes and pools which produced mosquitoes throughout the whole year. The conditions of a hot summer followed by a cold winter, which are characteristic of Macedonia and Palestine, no longer obtained, so that there was no winter cessation of infections.

It was unfortunate that such a place should have been the base of operations, for new troops arriving were constantly infected before they went up country, where the danger from mosquitoes was considerably less. And it was likewise unfortunate that no proper survey of the town was made immediately after the occupation in September 1916, with a view to selection of the most mosquito-free sites for camps. An area north of the inlet and bordering the sea was decidedly less infested with mosquitoes than the sites actually chosen for the concentration and other camps.

The mosquito nets used during the early part of the campaign were almost useless and, though a good deal of screening of buildings had been done by the Germans before the British occupation, so little was the value of this appreciated that much of it was destroyed by the British troops in order to obtain better ventilation.

Whatever was the cause, avoidable or not, the incidence of malaria amongst the troops was very high, for during the period 3rd June, 1916, to 27th October, 1917, the admissions for malaria were 3,036 officers and 104,666 men.

There was a mortality of 10 amongst the officers and 639 amongst the men. Malaria was responsible for 57·4 per cent. of the total admissions for sickness. Between 6th January, 1917 and 24th November, 1917, there were over 21,000 cases of malaria amongst the carriers, and other native formations suffered to a similar extent.

The mosquitoes chiefly responsible for malaria were the well-known African carriers *A. costalis* and *A. funestus*. *A. mauritianus* was also present, but is a doubtful carrier, while *A. squamosus* was of a very minor importance.* The breeding of these mosquitoes continued throughout the year, though possibly it was somewhat diminished during the dry weather. This limitation, however, must have been very slight, for in February, before the rains had commenced and at the end of the dry season, several hundreds of anophelines were collected in the vicinity of one of the camps.

There is no information of any value on the relative incidence of malignant tertian and benign tertian malaria during the campaign in East Africa.

Kilwa Kivinji and Kilwa Kisiwani, on the coast south of Dar-es-Salaam, and Tanga to the north were also highly malarious places. Inland the features of the country were a system of hills and valleys. The high land was relatively free from malaria. The valleys were hotbeds of the disease.

Anti-malaria work was not taken up seriously till the later phases of the military operations, and when it was commenced the troops had already been infected to a large extent. Malaria, in fact, practically ran riot in the early stages of the campaign, before adequate arrangements had been made for the protection of new arrivals from the moment they disembarked. Had such arrangements been possible the incidence of malaria in this campaign would undoubtedly have been materially less.

THE CAMEROONS.

Of the specific diseases malaria was the most important in the operations against the Cameroons. There were about 3,000 European troops in the various columns, and of the admissions at the Duala Base Hospital there were 613 for malaria during the 17 months of the campaign. This figure, however, represented only a fraction of the total malaria amongst the Europeans, for many did not come into hospital during the campaign.†

MESOPOTAMIA.

Malaria in Mesopotamia was not such a serious disease as in these other theatres of war. The admissions for the three years 1917, 1918 and 1919 were 6,723, 10,331 and 5,261 respectively. The great bulk of infections took place in the district between Basra and Kurna, but many infections occurred during the expedition into North Persia in 1918.

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* Dr. Mansfield Aders, of Zanzibar, has made a very useful mosquito survey of the country.

† See p. 306, Vol. 1, General History of the Medical Services.

The climate of Mesopotamia resembled that of Macedonia and Palestine in having a wet winter season and a dry summer. The winter, however, was not so cold and the summer was hotter. While mosquito breeding almost entirely ceased in winter, there was evidence that winter infection took place on a small scale. Thus of 232 cases admitted to a British general hospital during the period November to January, 1916–1917, 108 were recorded as primary infections, although mosquito breeding at this time was in abeyance.

The country is flat. In and around Basra, Kurna and other towns there are the palm tree plantations irrigated by channels from the Tigris or Shatt-el-Arab. The latter is tidal so that the creeks are filled and emptied at each tide, and it is probably on this account that mosquitoes were not more prevalent. Similar conditions existed at Nasiriyeh on the Euphrates. Apart from the rivers and the channels the country occupied by the expeditionary force was quite dry in the summer.

There was little malaria along the Tigris north of Kurna and the marshy stretch of river above Kurna, but the disease again appeared along the Diala river towards the Persian frontier. Mosquito breeding took place chiefly in pools formed along the channels. Many of the channels were full of water-plants which acted as dams.

Mesopotamia malarial surveys were carried out by Major Christophers, I.M.S. He found six species of anopheles: *A. pulcherrimus*, *A. stephensi*, *A. sinensis*, *A. lukisi*, *A. nursei* (*A. superpictus*), and *A. maculipennis*. The first is not an intense carrier though it was present sometimes in large numbers. *A. sinensis* is a marsh breeder, and it was seen in swarms in the marshy districts along the Euphrates between Kurna and Nasiriyeh. Fortunately, this district was unoccupied by troops save for a few isolated posts. It was not found to any extent in Basra or Kurna itself nor higher up the river. *A. lukisi* and *A. nursei* were only rarely seen and this is true also of *A. maculipennis*. The most dangerous mosquito was *A. stephensi*, a well-known carrier, and malaria was prevalent wherever it occurred.

As regards the race incidence of malaria the susceptibility of the British was greater than that of the Indian troops. The former had approximately the same number of cases as the latter, though they were only one-third the strength. The usual types of malaria were found, but, as in Macedonia and Palestine, only an occasional quartan parasite was seen. In October 1917, the percentage of malignant tertian cases was

56·7 for the Basra area. There was then a steady fall till April 1918, when only 16·9 per cent. were malignant tertian. The figure remained at about this level, with slight rises and falls, till August, after which there was a steady rise to 28·5 per cent. in January 1919.

For the Baghdad area in October 1917, the percentage for malignant tertian cases was 14·8, in November 29·2, and then it oscillated between 24·4 and 8·0 till July. After this there was a steady rise till in December it reached 56·4 with a fall in January to 38·2.* The marked rise in the Baghdad curve at the end of 1918 was due to the arrival of patients who had been evacuated from North Persia. Generally speaking, there was a rise in the proportion of malignant tertian cases towards the end of the year, but this was not nearly so marked as in Macedonia and Palestine.

Major Mackie, I.M.S., found *Anopheles nursei* in the area occupied by the Persian Force and by dissection proved it to be a carrier of malaria. *A. nursei*, however, is the same as the well-known carrier *A. superpictus* of Italy, Macedonia, Palestine, (*A. palestinensis*) and the Caucasus.

ITALY.

The malaria problem in Italy presented itself in the front-line area, at Taranto and also to a certain extent on the lines of communication, which were established for reinforcements to and evacuations from the Eastern Mediterranean and other theatres of war in the east by way of Taranto, in order to avoid sea transport.

In the front line there was very little malaria amongst British troops, though the Italian Army on the lower Piave front suffered heavily. From December 1917 to December 1918, inclusive, the British, with an average strength of about 78,000, had only 35 primary cases of malaria and 51 relapses. They were part of the 6th Italian Army which occupied the comparatively healthy Asiago plateau. The French troops in the same army had 73 primary and 140 relapse cases, and the Italians 150 and 331 respectively. In the mid Piave area the 8th Italian Army had 563 primary and 269 relapse cases, while on the lower Piave the 33rd Italian Army had 4,443 primary and 1,318 relapse cases.

On the lines of communication through Italy to Taranto, anopheles invaded the trains at many of the stopping places and infections took place there. There is no record of the extent of this, but it was noticed that anopheles were constantly brought to the Taranto camp by the trains. Attempts were made to regulate the stopping places so that the worst malaria areas could be passed through quickly, but the irregularities of the railway service rendered this impossible. The question of mosquito-proofing the trains was considered but was found to be impracticable.

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* These figures were compiled by Lieut.-Col. Ledingham, consulting bacteriologist to the Mesopotamian Force, and represent the results of the positive blood film examinations in the army laboratories.

At Taranto the troops exposed to infection, apart from those passing through the camp, numbered about 1,573 in 1917. Amongst these were 220 primary cases, of which 28 were evacuated to England and 6 died. The infection rate was 14 per cent. A labour detachment of 101 men arrived at the camp on 21st May, 1917, and by 15th November, 32 had been admitted to hospital with malaria. Later, four others contracted the infection, giving a malaria rate of 35 per cent. Another labour detachment of 96 men arrived on 17th September, and by the end of the year five had malaria, and by the following March four more. The sanitary section at Taranto received a draft of 31 men, only 25 of whom remained in the camp area. By the end of December six had gone down with malaria.

Troops, on their way to Salonika and Egypt, remained in the Taranto camp for a variable number of days before embarkation, and very soon complaints were received at Taranto that malaria infections were taking place amongst the men who had been there. As regards the prevalence of mosquitoes in the camp there are few records for 1917, but between 19th and 31st October, the entomologist, Sergeant Hargreaves, collected from 11 tents near the centre of the camp a daily average of three anophelines. Early in 1918 systematic collections were made in two areas. One was the camp area itself, and every hut, house or tent in this area was searched every day. The second area was outside the camp, and a series of eight houses was selected near the limit of the anti-mosquito operations. Daily collections were made. The first week of this work yielded 53 anophelines in the camp and 531 in the outer area. The numbers fell steadily till towards the end of April, and during May none were taken in the camp and very few outside. This fall was apparently due to the destruction of the hibernating mosquitoes before breeding had commenced. During May the anopheles leave their winter quarters to seek water on which to deposit their eggs. June showed a rise in the number collected, but the weekly number in the camp did not exceed 18, and in the outer area 110. During August and September there was a fall in the numbers, but at the end of September again a rise, so that for the two weeks ending 30th September and 7th October, 23 and 20 anopheles were taken in the camp and about 40 in the outer area. The numbers then fell to the end of the year.

The collections were continued during 1919 but the large numbers found at the beginning of 1918 ceased to appear. There was a steady fall until, during the summer, practically no anopheles were found in the camp, although a small number were collected in June and a larger number in September. It is important to note in this connection that the anopheles were being transported to the camp by the trains and nearly all the anopheles caught were in the huts and tents near the place where the trains stopped.

It was evident therefore that the anti-mosquito measures adopted in 1918 and 1919 practically kept the camp free from anopheles in 1919 and that the few which were found had been brought in by the trains. So free did the camp become that prophylactic quinine and the use of mosquito nets were discontinued. Amongst a personnel of over 1,000 in 1919 there were only nine possible camp infections, and it was probable that infection had been contracted elsewhere.

The mosquito breeding places were of the usual type; there were marshes, drains, pools and wells, and all of these were dealt with energetically by the well-known methods of mosquito destruction.

The prevalent mosquito was *A. maculipennis* which came chiefly from the ditches and marshes to the south and east of the camp, while *A. bifurcatus* was found to the west, where breeding places in the shape of troughs and wells occurred. *A. superpictus* was taken only once and was probably imported.

A number of dissections of anopheles was carried out in 1918 and 1919 with the following results :—

Source.	Stomachs.			Salivary Glands.		
	Exam.	Infect.	%.	Exam.	Infect.	%.
1918.						
Camp	122	19	15·0	119	3	2·0
House 14	97	3	3·0	73	1	1·25
Salina Grande	163	8	5·0	150	4	2·6
House 31	53	4	7·5	44	1	2·0
House 26 and Italian Anti-Aircraft Station.	514	40	8·0	519	3	·5
1919.						
Camp	269	22	8·1	272	—	—
Train	103	16	15·5	110	5	4·5
House 26	299	30	10·0	285	2	0·7
Other Houses	268	18	6·7	292	—	—

These figures are interesting in that they show a high degree of infection. It is difficult to explain this in the light of Wenyon's observations in Macedonia where at Lahanah village, which was known to be very malarious, a dissection of 2,910 anopheles yielded a very much lower incidence of infection.

The anti-malarial problem was much simpler in Taranto* than in Macedonia. The breeding places within the radius of the camp were limited and could be dealt with easily. In Macedonia on the other hand the breeding places were so extensive that it was impossible to deal with them all and the mosquitoes still persisted in such numbers that malaria could not be reduced to any great extent. Though the incidence of malaria was high in Taranto in 1917, the number of anopheles probably never reached more than a fraction of the numbers in such places as the Hortiak plateau in Macedonia, even after active measures for mosquito destruction had been carried out. Taranto and Macedonia may be regarded as two extremes. In the former anti-mosquito measures dispensed with the necessity of protective measures against the bites of mosquitoes, whereas in the latter protective measures had to take the place of mosquito destruction. Palestine, at least the line occupied before the advance on 21st September, 1918, occupied an intermediate position between these two extremes.

LIST OF MOSQUITOES COLLECTED AND IDENTIFIED IN THE VARIOUS WAR AREAS DURING 1914-1918.

MACEDONIA :—

Anopheles maculipennis, Mg.
Anopheles maculipennis, Mg., var.
Anopheles bifurcatus, L.
Anopheles plumbeus, Steph.
Anopheles hyrcanus, Pall. and var. *pseudopictus*, Grassi.
Anopheles algeriensis, Theo.
Anopheles superpictus, Grassi.
Stegomyia fasciata, F.
Ochlerotatus caspius, Pall.
Ochlerotatus pulchritarsis, Rond.
Ochlerotatus lepidonotus, Edw.
Ochlerotatus rusticus, Rossi.
Ochlerotatus detritus, Hal.
Ochlerotatus vexans, Mg.
Finlaya geniculata, Oliv.
Finlaya echinus, Edw.
Taeniorhynchus richiardii, Fic.
Theobaldia (*Allotheobaldia*) *longiareolata*, Macq.
Theobaldia annulata, Schrk.
Theobaldia (*Culicella*) *fumipennis*, Steph.
Theobaldia (*Culicella*) *morsitans*, Theo.

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* The work at Taranto is described in two reports by Colonel J. C. Robertson one for 1918 and the other for 1919. The report for 1918 appears in full in the *Journal of the Royal Army Medical Corps* for May 1920.

MOSQUITOES—*cont.*

MACEDONIA—*cont.*

Culex pipiens, L.
Culex hortensis, Fic.
Culex mimeticus, Noé.
Culex apicalis, Adams.
Culex modestus, Fic.
Culex tipuliformis, Theo.
Culex univittatus, Theo.
Uranotaenia unguiculata, Edw.

PALESTINE :—

Anopheles maculipennis, Mg., var.
Anopheles bifurcatus, L.
Anopheles superpictus, Grassi.
Anopheles culicifacies Giles var. *sergenti*, Theo.
Anopheles multicolor, Camb.
Anopheles pharoensis, Theo.
Anopheles hyrcanus, Pall.
Anopheles mauritianus, Grandpré.
Anopheles algeriensis, Theo.
Stegomyia fasciata, F.
Ochlerotatus caspius, Pall.
Ochlerotatus detritus, Hal.
Ochlerotatus mariae, Serg.
Theobaldia (*Allotheobaldia*) *longiareolata*, Macq.
Theobaldia annulata, Schrk. and var. *subochrea*, Edw.
Theobaldia (*culicella*) *morsitans*, Theo.
Taeniorhynchus richiardii, Fic.
Uranotaenia unguiculata, Edw.
Culex pipiens, L.
Culex hortensis, Fic.
Culex mimeticus, Noé.
Culex tipuliformis, Theo.
Culex univittatus, Theo.
Culex laticinctus, Edw.

MESOPOTAMIA :—

Anopheles stephensi, Liston.
Anopheles pulcherrimus, Theo.
Anopheles hyrcanus, Pall.
Anopheles algeriensis, Theo.
Anopheles superpictus, Grassi.
Anopheles maculipennis, Mg., var.
Stegomyia fasciata, Mg.
Ochlerotatus caspius, Pall.
Theobaldia (*Allotheobaldia*) *longiareolata*, Macq.
Culex modestus, Fic.
Culex tritaeniorhynchus, Giles.
Culex fatigans, Wied.
Culex tipuliformis, Theo.
Culex pipiens, L.

NORTH WEST PERSIA :—

Anopheles superpictus, Grassi.
Anopheles maculipennis, Mg.
Ochlerotatus caspius, Pall.
Ochlerotatus vexans, Mg.
Culex pipiens, L.
Culex tipuliformis, Theo.

MOSQUITOES—*cont.*

NORTH RUSSIA :—

Anopheles maculipennis, Mg.
Theobaldia arctica, Edw.
Ochlerotatus lutescens, F.
Ochlerotatus alpinus, L.
Ochlerotatus, sp.

ITALY :—

Anopheles maculipennis, Mg.
Anopheles bifurcatus, L.
Anopheles algeriensis, Theo.
Ochlerotatus caspius, Pall.
Ochlerotatus caspius, Pall. var. *hargreavesi*, Edw.
Ochlerotatus detritus, Hal.
Ochlerotatus vexans, Mg.
Ochlerotatus rusticus, Rossi.
Ochlerotatus nemorosus, Mg.
Ochlerotatus pulchritarsis, Rond.
Theobaldia annulata, Schrk.
Theobaldia (*Allotheobaldia*) *longiareolata*, Macq.
Culex hortensis, Fic.
Culex pipiens, L.
Culex univittatus, Theo.
Uranotaenia unguiculata, Edw.

TANGANYIKA TERRITORY :—

Anopheles costalis, Lw.
Anopheles funestus, Giles.
Anopheles mauritianus, Grandpré.
Anopheles squamosus, Theo.
Anopheles maculipalpis, Giles.
Skusea pembaensis, Theo.
Stegomyia fasciata, F.
Culex fatigans, Wied.
Culex watti, Edw.
Culex sitiens, Wied.
Culex aurantapex, Edw.
Culex bitaeniorhynchus, Giles.
Culex duttoni, Theo.
Culex consimilis, Newst.
Culex tigripes, Grp.
Eretmopodites chrysogaster, Graham.
Megarhinus (*Toxorhynchites*) *brevipalpis*, Theo.

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CHAPTER X.

MALARIA—(*continued*).

PATHOLOGY, SYMPTOMS, DIAGNOSIS AND TREATMENT.

WITH regard to the pathology of malaria, the interest has mainly centred round the subtertian infection. The suddenness with which death may occur has been much commented upon. It is recorded by Dudgeon that out of the number of fatal cases in Salonika, 57 per cent. died within two days of admission to hospital. Many died of acute heart failure. Out of 50 post-mortem examinations in this disease in Palestine, 10 died from right heart failure, an equal number with cerebral complications, 7 with hæmolytic icterus, 3 from hyperpyrexia, while 13 were complicated by pneumonia and the remaining 7 by co-existing infections, such as bacillary and amœbic dysentery.

Malaria-stricken patients were specially liable to contract other virulent infections, and of these the chief appears to have been influenzal broncho-pneumonia. This was a specially fatal complication, and it is recorded that out of 797 deaths from malignant malaria in Palestine and Syria towards the end of 1918, no less than 62·5 per cent. were due to the influenzal broncho-pneumonia then sweeping through the country. This complication was not commonly noted before the middle of October 1918.

As an explanation of the sudden fatalities in uncomplicated subtertian malaria, Dudgeon and Clarke have described a fine, fatty degeneration of the heart muscle akin to that of a diphtheritic toxæmia. The adrenal glands showed congestion and loss of characteristic lipoids, together with thrombosis and necrosis of the cortex.

In the spleen, extreme congestion and excessive phagocytosis of red blood cells were always observed and necrosis of the pulp tissue, especially of the Malpighian corpuscles, was also noted.

The liver and kidneys also showed focal necroses and deposition of pigment in large clumps, and, according to Wenyon's observations, these appearances are associated in the former organ with a corresponding increase in the production of bilirubin.

The brain in fatal coma showed extensive thrombosis, especially of the vessels in the white matter, degeneration of nerve cells and blockage of the capillaries with parasites.

In certain cases of coma energetically treated with quinine during life, no parasites were found in the brain capillaries, but a considerable œdema of the brain substance and an increase in the cerebro-spinal fluid were noted, possibly due to the action upon and absorption by the cerebral substance of a circulating malaria toxin. So often was death noted in cases completely cinchonised, in which no parasites could be found after death in any of the tissues or bone-marrow, that the existence of a malarial toxæmia, as opposed to the hitherto accepted theory of a mechanical obstruction of the capillaries by the sporulating subtertian parasite, must be considered as a possible cause of death.

In the intestines of algid or abdominal cases, congestion, petechial hæmorrhages and scattered necroses of the mucosa have been noted.

Great variation in the size of the spleen and in the number of contained parasites has been noted in these fatal cases. The spleen is generally engorged and contains a dark and diffluent pulp ; the capsule is stretched and shiny and the whole organ may weigh two pounds or more ; lymphoid flakes and evidences of perisplenitis may be present. On the other hand, fatal cases have been seen with only a slight enlargement of the spleen, with a firm dark red pulp, a few contained parasites and scattered pigment. The toxicity of these parasites in different individuals must therefore vary considerably. Spontaneous rupture of the engorged spleen with sudden death was noted in Mesopotamia, Macedonia and Palestine ; this may have been due to infarction or to rupture of the capsule.

Symptoms.

The cases which occurred during the war presented little that was new in the clinical aspects of benign tertian malaria. Primary infections especially were for the most part typical, with a rapid rise of pyrexia, rigors and an equally rapid fall. Higher degrees of pyrexia (temp. 105°-106° F.) were almost invariably recorded than in the subtertian form. There is scarcely any other epidemic pyrexia, with the exception of sand-fly fever, with which this infection may, from a clinical point of view, be confused.

Observations upon the remarkable periodicity which the benign infection exhibits tended to show that the attacks were more liable to occur in the earlier hours of the day.

Tertian periodic pyrexias were found to be due to one generation, quotidian pyrexias to two generations of the parasite. Severe and alarming symptoms, and even coma, were observed in benign tertian cases, especially in Macedonia, but generally, when they occurred, they were caused by a double infection with the subtertian parasite.

Quartan infections occurred so rarely amongst British troops as to preclude any extensive observations being made ; usually unsuspected on clinical grounds, they were recognised quite accidentally by microscopic examination.

The pleomorphism which subtertian infections may exhibit and the many medical and surgical conditions they may simulate, has attracted a considerable amount of attention. It is not surprising that many medical officers new to the tropics failed to recognise the true nature of the disease ; the wonder is rather that mistakes in diagnosis were so few.

There is considerable danger, wherever malaria is prevalent, of a tendency to make a diagnosis of malaria too readily in doubtful cases. Thus Phear records that such diverse conditions as cerebral abscess, meningitis, hepatic abscess, peritonitis from different causes, and even suppurative peritonitis, were found at autopsy in cases which were suspected of being purely malarial in nature. It should be emphasised that, wherever a blood film diagnosis of malaria will not fully explain the clinical picture, other possible causes of the illness should be carefully considered and assistance sought in a leucocyte count.

On the other hand, in the absence of laboratory diagnosis or where such facilities are not fully used, malignant malaria provides many pitfalls for the unwary owing to the diversity of symptoms which it may exhibit. The tendency is for the clinician, after a fatality has once occurred, to disregard clinical symptoms altogether and to trust too much to the laboratory for diagnosis.

Malignant tertian fever, which is caused by the subtertian parasite, in general may be extremely mild, fairly severe, or in a small percentage of cases fulminating in character. Many dramatic deaths were recorded. The suddenness with which death might take place had to be seen to be realized ; men have fallen out and died while on the march, and in several instances the fatal illness lasted only a few hours.

Compared with the benign infections, malignant malaria was less sudden in its onset ; more usually it was insidious, and the pyrexia might not be so marked or subject to such sudden intermissions. For the first five days of a primary infection, a gradual steppage rise of a remittent pyrexia resembling that of enteric was quite commonly observed. Rigors might be entirely absent. There might be no subjective symptoms, save headache and an aching in the bones. On the other hand it is known that parasites may be present in the peripheral blood in quite considerable numbers without any history of malaise or fever at all. Such cases were recorded from Macedonia and from the Jordan valley.

The number of parasites in the peripheral blood did not appear as a general rule to bear any relation to the severity of the clinical symptoms. This is probably due to the method of sporulation in the capillaries of the internal organs. Coma and death occurred in cases which showed but scanty rings in the peripheral blood, and conversely patients were seen who had a very heavy blood infection with but few concomitant symptoms.

The double crisis of temperature which this disease exhibits in its typical form was not always discernible and should, therefore, not be too much relied upon in diagnosis.

The subtertian parasite produces symptoms by mechanical blockage or by toxæmia. In the first method sporulation in some particular organ causes a blood stasis or partial thrombosis, and may give rise to all kinds of local symptoms ; in the second there are general symptoms due to a diffuse toxæmia.

During the war it was realised that splenomegaly is not an integral part of a malarial infection. It is only after repeated infections and relapses that the spleen becomes large enough to be palpated. It was remarked that in only a small percentage of cases, microscopically diagnosed, was the spleen at all palpable. Too great weight should not be given to percussion of the splenic area as a means of ascertaining enlargement of the organ ; on the other hand, there was usually a considerable degree of pain and tenderness over the splenic area during the attack of fever.

The clinical types of subtertian malaria may be classified and described according to the organs upon which the stress of infection fell.

Psychical disturbances due to toxæmia, or cerebral irritation produced by the subtertian parasite take the form of delirium, acute mania, or delusional insanity, with a tendency to suicide. The mental state and muscular inco-ordination closely resemble that produced by alcohol ; there were several instances of men being arrested as either drunk or mentally deranged, and even sent down from the firing line under guard, who were found to be suffering from a malarial infection.

Hæmorrhages into the motor area produce monoplegia or diplegia or, if into the internal capsule, complete hemiplegia ; pontine lesions with crossed paralysis have been recorded. The effects of these lesions were sometimes permanent. The hyperpyrexia associated with cerebral disturbance closely resembled that of heat stroke. Unilateral epileptiform convulsions produced by cerebral irritation simulated those of a Jacksonian epilepsy, and in these cases the parasites might be very scanty in the peripheral blood. Spinal pains combined with cerebral symptoms, head retraction and rigidity of neck muscles might arouse the suspicion of a cerebro-spinal meningitis.

Cases with profuse vomiting, or even actual hæmatemesis were noted. Where the pain was very severe, intestinal obstruction might be suspected, or the patient might present the picture of acute hæmorrhagic pancreatitis.

Malignant malaria sometimes resembled certain surgical conditions ; pain over the liver or gall bladder, with fever, was quite commonly mistaken for cholecystitis. Appendicular pain might closely simulate surgical appendicitis, and it is recorded that in Salonika, and elsewhere, this mistake not infrequently occurred. The pain in such cases might be strictly localized to McBurney's point, and therefore in doubtful cases the surgeon should exclude malaria by means of a blood examination and a leucocyte count.

Enteritis of varying degrees of severity was commonly observed in subtertian infections and might focus the attention of the clinician entirely on the alimentary tract. The thrombosis and the toxæmia might produce petechiæ and hæmorrhages, which, if they were into the intestinal canal, might cause symptoms resembling those of dysentery.

Algid cases with subnormal temperatures and collapse were commonly observed ; if associated with vomiting, profuse and watery diarrhœa, they simulated cholera.

Several authorities, including Falconer and Anderson, believe that a purely malarial infection can produce symptoms and physical signs of bronchitis, pulmonary congestion and consolidation. Most clinicians noted the frequency of pulmonary complications with subtertian infections, but the majority regarded actual consolidation as being due to a secondary infection with the pneumococcus. Whether pleurisy or pleuritic adhesions can be produced by the same means is open to doubt. Generally speaking, a splenic pain, due to distension of the organ by malaria, is referred to the pleura and may thus give rise to pain in this region.

Cases with joint effusions closely resembling acute rheumatism were recorded ; the bone pains accompanying the pyrexia might suggest rheumatism, or more commonly a tentative diagnosis of influenza ; it was remarkable how frequently this mistake occurred.

The pyrexia of subtertian malaria is apt to be regarded at first as one of the commoner pyrexias. The remittent temperature, especially during the first week, simulated that of enterica ; and the clinical differentiation from relapsing fever, especially the North African type, might be impossible on clinical grounds alone.

Hæmorrhages occurred into the skin in acute subtertian cases and sometimes produced lesions similar to those of purpura hæmorrhagica, typhus, or even measles, and occasionally led to mistakes in diagnosis.

General œdema with ascites due to subtertian malaria without albuminuria was occasionally seen both in Salonika and in Palestine. A general œdema of the face and extremities, yielding to quinine, occurred among the German prisoners from Palestine. Certain cases closely resembled acute nephritis, the urine containing blood and renal epithelial cells. Occasionally lumbar pain was associated with hæmaturia in an uncomplicated subtertian infection.

A high remittent temperature with icterus is known as the bilious remittent form of subtertian malaria. The hæmolytic icterus thus produced may be very striking and resemble that of yellow fever ; it is often associated with a profuse bilious vomit. The tendency was to mistake this form for obstructive jaundice with pyrexia, or for the malignant jaundice of *Spirochætosis icterohæmorrhagica*. The lesson to be learnt from this is that repeated blood examinations should be made in every case of jaundice occurring in malarial districts.

The disturbance in cardiac rhythm might be mistaken for disordered action of the heart. The vasomotor changes, such as arterial spasm, were sometimes important. Thus gangrene of the feet due to this cause was observed in Salonika.

The most important sequelæ were cachexia and anæmia. The debility produced might be considerable and the anæmia might reach a high degree. The hæmoglobin might be reduced to one-half or even one-third and the cells to 1,000,000 or less. Splenomegaly was nearly always present. A very great degree of anæmia with general anasarca was noted especially amongst Turkish prisoners from Arabia who were very heavily infected with malaria. The debility and anæmia following a primary infection may rapidly produce a cachectic condition especially in young soldiers. This condition has been referred to by James under the designation of acute primary cachexia.

Post-malarial anæmia was generally of the pernicious type with poikilocytes, megaloblasts, and even myelocytes ; in fact it might resemble pernicious anæmia or leucocythæmia very closely indeed, but the extreme changes in the white cells which occur in the latter disease were never seen. In other cases there was an aplastic anæmia with little or no attempt at red cell regeneration.

A large proportion of cases of disordered cardiac action with unduly sensitive exercise response was attributable to malaria; this is possibly due to the specific action of malarial toxins upon the myocardium.

In addition to cases of peripheral or central lesions, the influence of subtertian malaria as a contributory factor in functional disorders of the brain was generally recognized in Salonika. The commonest type of psychosis following malaria was some form of mental confusion or depression, which fortunately was not permanent. In a few instances a peculiar mental disorder with obliteration of all sense of time and space, known as Korsakoff's syndrome, supervened. There was no evidence that a true malarial neuritis exists.

Finally, the tendency of subtertian infections to develop blackwater fever, especially during the winter season, must always be borne in mind. The relationship between these two conditions is very close, and Parsons and Forbes from clinical observations in Salonika show that a transient hæmoglobinuria takes place quite commonly in an otherwise uncomplicated subtertian infection.

Both the subtertian and the benign forms of malaria are liable to be complicated by other diseases. The most frequent of these in the war was some form of dysentery, most usually of the bacillary type. When co-existing with a primary subtertian attack the prognosis was grave. Many pulmonary infections were prone to supervene; sometimes it was a lobar pneumonia, and the extent and virulence of influenzal broncho-pneumonia as a cause of death has already been noted. Malaria was especially prone to co-exist with and complicate an abscess of the liver. Its liability to occur in association with enteric has long been recognized.

It was pointed out during the war that malaria subjects were prone to develop a pulmonary tuberculosis or that latent tubercular infections might become active during the course of the disease.

Diagnosis.

The clinical forms of subtertian malaria and the diseases which it might simulate may be summarized as follows:—

Type of Subtertian Malaria.	*Diseases simulated.*
Cerebral forms.	
Comatose	Coma of various kinds, especially alcoholic or traumatic.
Coma with hyperpyrexia	Sunstroke or heatstroke.
Maniacal or delirious with suicidal tendency.	Lunacy or mania; acute typhus.
Epileptiform	Jacksonian epilepsy.
Cerebro-spinal	Cerebro-spinal meningitis.

Abdominal forms.	
Malarial enteritis with hæmorrhage	Acute dysentery.
Algid with subnormal temperature and collapse.	Cholera or paracholera.
Obstructive	Appendicitis, cholecystitis, acute pancreatitis, intestinal obstruction.
Pulmonary forms.	
Bronchitic	Broncho-pneumonia.
Pneumonic	Pneumonia.
Pleuritic	Pleurisy.
Types of average severity.	
Influenzal or rheumatic, with pyrexia and joint pains.	Influenza ; acute rheumatism.
Enteric-like	Enterica, sand-fly fever, trench fever, relapsing fever, and hepatic abscess.
Cutaneous forms.	
Cases with multiple petechiæ	Typhus, purpura or measles.
Nephritic forms with œdema.	
Cases with albumen and cells in urine.	Acute nephritis.
General œdema without albumen and sometimes ascites.	Cardiac failure or war œdema.
Icteric forms.	
Bilious remittent type with bilious vomit and hæmolytic icterus.	Weil's disease, yellow fever, obstructive jaundice.
Sequelæ.	
Cachexia and anæmia	Pernicious anæmia, leucocythæmia, pulmonary tuberculosis, debility.
Blackwater fever	Quinine hæmoglobinuria and paroxysmal hæmoglobinuria.
Neurasthenia and mental confusion	Insanity.

The experiences of the war disclosed little new with regard to the microscopic diagnosis of malaria. The mechanism ought to be near at hand ; a microscope, and a pathologist skilled in its use, ought to be an integral part of a field ambulance in a malaria-stricken country. The clinical symptoms of malaria being of so protean a character, clinical diagnosis must always be supplemented by that of the microscope. Special malaria diagnosis units, consisting of one officer and two men with the necessary transport and light equipment with two microscopes and essential stains, proved to be the most satisfactory means of dealing with this aspect of the subject in Palestine. Being extremely mobile and independent, such a unit could be moved to any part of the field of operations and attached to a field ambulance wherever its services were most required. It is essential that both the officers and men should be specially trained in the microscopic diagnosis of malaria.

For rapid work and satisfactory results, provided an ample supply of neutral distilled water is obtainable, no stain has yet been found to surpass Leishman's. The adoption of the thick film method is said to have resulted in East and South Africa in improving the accuracy of diagnosis by 50 per cent.

It undoubtedly has the advantage of showing up the parasites, especially crescents, in the peripheral blood, but against this a considerable amount of difficulty is at first experienced in recognizing the stage and the species of the parasite owing to the distortion which takes place during dehæmoglobinization. The technique is the same as that detailed for the detection of spirochaetes in African relapsing fever.*

The thick-film method also has the advantage of showing up spirochaetes of relapsing fever, if these are present.

Failures with Leishman's stain are generally due to over-fixation with the raw stain or over-action in its diluted state. Probably half a minute is quite sufficient for fixation with the raw stain and two and a half minutes when subsequently diluted with three times its amount of distilled water.

In differentiation of the two forms of parasite, too much reliance should not be placed on the presence of Schüffner's dots in benign tertian malaria; they are often absent in the early stages of infection. Much more attention should be paid to the character of the ring and the enlargement of the infected corpuscle.

Whatever method of making films is adopted, the thick or the thin film, or a combination of both, it is advisable in a suspicious case that at least three films of the patient's blood be examined on three separate occasions before a diagnosis of malaria is definitely negatived. One should remember that a severe clinical subtertian infection may be associated with scanty parasites in the peripheral blood.

On no account, if it can be avoided, should the microscopic diagnosis of malaria be relegated entirely to casualty clearing stations and base hospitals; the nearer it is carried out to the seat of actual operations the better.

Attempts have been made to improve diagnosis by a complement deviation method in the latent phases of malaria, and experiments in this direction have been made by Thomson, using antigens prepared both from splenic extracts and artificial blood cultures of the parasites dissolved in dilute caustic soda. The results have hitherto been somewhat indefinite.

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* *See* Chapter XIV, p. 339.

As regards the rise of mononuclear leucocytes which supervenes after a malaria attack, although abundant confirmation has been forthcoming of a rise above 15 per cent. immediately following the pyrexia, the value of this method in ascertaining a latent infection, as, for instance, in pensionable men, is being seriously discredited as a means of arriving at a diagnosis. It has been shown by Thomson that the mononuclear rise varies inversely with the temperature ; when the temperature is rising the number of mononuclears in the peripheral blood is falling, and when the temperature falls the mononuclears increase.

During the height of the paroxysm there is a leucopenia of 2,000 leucocytes per c.mm., followed by a post-malarial leucocytosis.

Treatment.

During the war unparalleled opportunities presented themselves for testing various forms of treatment of malaria. Continuous observations were possible upon large numbers of disciplined men, and the results obtained were minutely recorded, especially in Salonika and in the United Kingdom. Little, however, that is new in the treatment of malaria has been ascertained. The whole treatment may still be summed up in the one word—quinine. But from the maze of literature upon this subject one indisputable fact emerges ; namely, that quinine is by no means the specific drug it was formerly supposed to be. It is not to be inferred that belief is waning in its curative powers, but there are serious doubts in many minds of its power of preventing relapses, more especially in benign infections.

As quinine is the only drug that acts efficiently upon the malaria parasite, its administration should be begun directly a diagnosis is obtained, quite irrespective of the stage of the attack or of the degree of pyrexia ; but in order that the full benefit may be obtained, it is essential that the drug should be absorbed by the stomach and intestines. Should there be any intestinal stasis, should digestion be in any way disarranged, or the intestinal mucosa become covered with mucus, absorption of quinine will only be partial.

A preliminary purge of calomel (grains 3–5) or of blue pill (4 grains), followed by a saline aperient, should invariably precede the administration of the quinine. The drug should always be given in dilute solution and in a mixture which will render the taste less unpleasant. Syrup of orange (drachm 1) will disguise the taste to a certain extent. This is said to be also the case if glycerine is added to the mixture, or if the quinine is dissolved in milk. In military practice, if tabloids have to be substituted for a mixture, chewing of a piece of bread to a great extent removes the unpleasant taste.

Wherever possible, quinine should be given by the mouth, as experience showed that it is as quickly absorbed by the alimentary as by any other route. In the acute stage of the disease, where a tendency to nausea and vomiting exists, all diet, even milk, should be withheld, but the patient should be encouraged to drink freely of water and especially hot decoction of lemon. This is made from four slices of lemon, including the peel, with a teaspoonful of sugar to 8 ozs. of water. It assists the absorption of the drug.

The dosage of quinine should not be less than 30 grains, or exceed 45 in the twenty-four hours. The most soluble salts should always be used wherever possible. Of these the bi-hydrochloride is the most soluble, the hydrochloride most nearly approximates it, while the sulphate is the least soluble. For ordinary purposes the hydrochloride is to be preferred ; it should be given in 10-grain doses, dissolved in 2 ozs. of water, three times a day, at four-hourly intervals, and it is undoubtedly more quickly absorbed by an empty stomach. Most authorities are agreed that heroic doses of 80 to 100 grains in twenty-four hours were not more effectual than the smaller ones. If the sulphate or bi-sulphate is used, a certain amount of acid must be added in order to dissolve the drug completely ; the proportion being 2 minims of dilute sulphuric acid to every 10 grains of quinine. The patient should be put to bed, at any rate for the first week, as rest is essential.

In benign tertian and subtertian infections of average severity it is advisable to continue the full dosage of quinine for some considerable time, at any rate for 21 days, in order to prevent a relapse ; and the experience gained during the war showed that it was advisable to continue it, in 10-grain doses, every day for the subsequent three months. Symptoms of cinchonism may develop, but unless severe and continued, are not serious. For the tinnitus so produced the quinine should be dissolved in hydrobromic acid, or one of the bromides should be prescribed as in the following prescription :—

Hydrochloride of quinine	grains 10
Dilute hydrobromic acid	minims 30
Syrup of orange	drachm 1
Water	to half an oz.

If vomiting is troublesome, a teaspoonful of bicarbonate of soda in warm water should be given at the same time, and if rejected, the dose of quinine should be repeated; if very severe, the stomach should be washed out with small doses of tincture of iodine (30 minims to the pint) and counter-irritation applied to the epigastrium. Wherever possible there appears to be a distinct advantage in giving quinine in small doses of 5 grains each, six times during the day.

Other measures are of course necessary. During the cold stage, hot water bottles must be applied ; during the hot stage, it may be necessary to sponge the patient frequently with warm water in order to reduce the pyrexia, and to give copious draughts of lemonade to assist perspiration. Diaphoresis may be promoted by prescribing the following mixture :—

Solution of acetate of ammonia	drachms	2
Spirit of nitrous ether	minims	30
Camphor water	to half an oz.	

For the headache, caffeine, aspirin or phenacetin (10 grains) may be used.

A large tender spleen may often incite vomiting, and the pain, which may become severe, becomes less apparent after the application of a mustard plaster or of a hot fomentation, the patient being instructed to lie on the left side.

During the second week of treatment quinine is better borne when given in an effervescing form, as in the following prescription :—

Quinine hydrochloride	grains	10
Citric acid	,,	20

mixed together in powder form and taken with the following mixture :—

Carbonate of ammonia	grains	20
Carbonate of potash	,,	20
Water	to half an oz.	

In men who bear quinine badly it is better tolerated if given with small doses of opium, as in the preparation known as Warburg's tincture, which contains aloes, opium (1 in 4,000), rhubarb, camphor and a number of other herbs, in doses of 1 oz. every four hours continued for four or five days.

In the management of a malaria case the clinician should be guided by frequent microscopic blood examinations, and more especially is this necessary should any untoward symptoms occur after the primary pyrexial period is passed.

In the care and after-treatment of a malaria case it is essential that due consideration should be given to the question of food. clothing and avoidance of over-exertion. Soldiers should be hardened by graduated exercise while in convalescent camps especially set aside for the purpose, a practice which obtained recognition during the war. Convalescence should last at least three weeks. The administration of quinine should by no means be neglected, and a daily parade for this purpose should be held at an appointed hour.

In order to counteract the anæmia produced by malaria, and in order, in the opinion of many, to aid in the absorption of quinine, arsenic should be given from the onset, either in the form of liquor arsenicalis (minims 5) thrice daily, or in the form of a mixture combined with iron as in the following prescription :—

Acid solution of arsenic	minims	3
Ferrous sulphate	grains	2
Dilute hydrochloric acid	minims	3
Water	to half an oz.	

In military practice it is more convenient to prescribe the iron and arsenic together in pill form, which should be given twice daily. Strychnine may be added as in the following prescription :—

Iron hypophosphite	grains	2
Arsenious acid	grain	$^{1}/_{50}$th
Strychnine sulphate	grain	$^{1}/_{50}$th
Saccharine	grain	$^{1}/_{100}$th

As regards the treatment of the two main forms of malaria the following general statements may be made.

In benign tertian infections the individual attack is easily dealt with, the asexual parasites normally disappearing from the blood in four days, but the patient is liable to parasitic and clinical relapses for a long period and complete eradication of the parasite from the system is very difficult. The same rules hold good for the quartan infections which were occasionally found during the war.

In subtertian infections, the individual attack is considerably more resistant to quinine, the asexual parasite remaining in the blood for four days on the average, the longest period noted being thirteen days. The patient will be cured in a large number of cases in the first treatment, if it is conscientiously carried out, and especially if followed by the administration of quinine for the prevention of relapses, the liability to relapse being much less than in the benign tertian. But, further, the thorough treatment of subtertian or malignant infections is more important than that of the benign form, owing to the alarming clinical manifestations which may supervene.

Should the number of parasites present in the peripheral blood be great, the patient mentally confused, the tongue unduly furred, hyperpyrexia supervene, the spleen and liver be enlarged and tender or vomiting be excessive, should in fact any unfavourable symptoms manifest themselves* in spite of oral treatment with quinine, recourse must be had to other methods of quinine administration, and of these the intramuscular route has been the one most practised.

With regard to the advantages and disadvantages of this method, the observations of Dudgeon and Manson-Bahr at numerous autopsies showed, what had long been recognized, that quinine is undoubtedly a tissue poison and that it probably causes a slight degree of muscle necrosis in every case, but if given wisely or in not too concentrated a form and at definite intervals no real danger is likely to ensue. On the other hand in a patient unduly debilitated and wasted, whose powers of resistance are small, a more extensive tissue necrosis is liable to occur than in a normal individual ; furthermore, Fairley and Dew have shown that hæmatogenous septic infections are likely to ensue in these individuals owing to the absence of any leucoblastic response in the bone marrow, and such an infection will set alight any necrotic patch in the muscular tissue. Manson-Bahr's experiences corroborated this observation. Great caution should therefore be observed in injecting quinine in debilitated subjects.

In some cases a considerable fibromyositis may occur from injections of quinine involving the sciatic nerve with consequent paralysis of the corresponding leg. This and more severe consequences, such as supervention of general sepsis, gas gangrene, extensive hæmorrhages into the tissues through implication of a large vessel, spreading œdema and widespread tissue necrosis leading to abscess, have all been recorded as the result of too vigorous treatment by intramuscular injections, but it is doubtful whether these unfortunate occurrences outweigh the undoubted clinical improvement which has followed the adoption of this method.

Every care must be taken to maintain asepsis in the operation, and due consideration must be paid to the anatomical structures of the part chosen for injection.

The site of injection is preferably the muscles of the buttocks on the line of, and a hand's breadth posterior to, the great trochanter ; a stout needle should be used and the injection made deep into the gluteal muscles, but on no account should the quinine solution impinge upon the ilium, and care must be taken to avoid the course of any important nerve. The effect of the injection and its absorption may be increased by massage.

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* Mental or other grave symptoms coming on suddenly in the course of a benign tertian infection have usually been due to a co-existing infection with the subtertian parasite, which, owing to the peculiar method of sporulation in the capillaries of the internal organs, may have been at first overlooked on microscopical examination.

The salt of quinine employed for the purpose should be the most soluble—the bi-hydrochloride, in the proportion of 6 grains to the c.c. of distilled water. It is best to give two injections daily for three consecutive days, supplementing them if possible by quinine administered orally. Some clinical workers, such as Phear in Macedonia, advise 40 grains in the 24 hours till all alarming symptoms have disappeared. Experience at autopsy has shown that, even with the more moderate doses recommended above, a complete disappearance of the asexual parasites from the blood and internal organs takes place subsequent to the injection of 36 grains.

This method obtained a considerable degree of approval from clinicians especially in Salonika. It has, however, its limitations and it is open to abuse, the chief of which is the tendency to continue intramuscular injections repeatedly, in the circumscribed area, when all indications for their administration, as judged by microscopic blood examination, have disappeared. It is useless to continue to inject quinine after all parasites have disappeared from the circulation. In certain cases of benign tertian infection where oral quinine is ineffective in reducing the temperature, a few intramuscular injections have been followed by good results. One point, the importance of which is apt to be overlooked, is that routine intramuscular injection of quinine in all serious cases of subtertian malaria ensures its retention and absorption at the earliest possible moment and therefore may prevent pernicious symptoms supervening. Quinine thus administered undoubtedly saved many lives, and further it probably increased the chances of effecting a permanent cure of the disease.

The intravenous method of quinine administration is advocated in severe cases of cerebral malaria with coma or convulsions, or where such complications are threatening; it may also be used in the algid and choleraic forms.

The injection should be made into the median basilic or cephalic vein at the bend of the elbow, with a 10 c.c. syringe provided with a sharp needle. It is advantageous to make the vessels prominent by constriction with a rubber tube or an elastic bandage. On entry into the vein the piston should be slightly withdrawn so as to allow some blood to flow back into the barrel; it is then safe to proceed with the injection, which should be made slowly, three minutes at least being taken over the operation.

The best concentration of quinine would appear to be 10 grains of the bi-hydrochloride dissolved in 10 c.c. of normal saline. Sometimes it is necessary to repeat the injection, and in Salonika in exceptional cases as many as 60 grains were given in the twenty-four hours by this method. As a rule, however, smaller doses sufficed. In an apparently hopeless case it is probably better to supplement intravenous by intramuscular injections. Apparently there is no object in unduly diluting the quinine, for, in the opinion of many, this greatly increases the consequent reaction.

As regards the dangers of intravenous administration of quinine, alarming symptoms of reaction and even sudden death may ensue in pernicious subtertian cases, presenting cardiac or pulmonary distress. In such cases it is better to proceed by the intramuscular route. Finally, there is evidence that a coma which persists after the disappearance of parasites from the peripheral blood may be due to increased intra-thecal pressure, and, for this, repeated lumbar puncture and withdrawal of cerebro-spinal fluid has been practised with advantage.

Kerr and Turnbull after extensive observation concluded that intravenous injection of large doses of bi-hydrochloride of quinine in benign tertian infections caused not only a rapid improvement in the patient's general condition but also prevented further relapses. Unfortunately, further experience has not confirmed these apparently favourable results. Quinine injection by the rectum was employed at times during the war, but by no means obtained universal approbation. It is given in doses of 10 to 40 grains dissolved in 10 to 20 ounces of saline. The method proved of value as a means of temporarily supplementing the amount of quinine introduced by other channels.

Subcutaneous injection of quinine was practised in Macedonia by the French, and was to a certain extent employed in East Africa. The hydrochloride of quinine was used by the French in combination with urethane in doses of 7 grains of the former with 2 grains of the latter. Sloughing of the skin was occasionally observed, and possibly the method possessed no advantage over the intramuscular route, besides being much more tedious.

In addition to intramuscular and intravenous methods of administering quinine for the treatment of pernicious symptoms of subtertian malaria, attempts may be made to lessen the malarial toxæmia by abstraction of a considerable amount of venous blood, one pint or more, and the injection of a corresponding quantity of normal saline; but this is a method which requires further investigation.

Though quinine given in moderate doses has a distinct influence upon the gametocytes of benign tertian malaria, it acts less strikingly upon the crescent forms of the subtertian. In full doses of 30 grains of quinine a day it was shown that these forms take a period of three weeks or more to disappear from the peripheral blood. Therefore, in such cases full doses of quinine should be given for at least that period.

Malarial cachectics, with anæmia and large spleen, emaciation and a low form of pyrexia, require to be treated with full doses of iron, arsenic and quinine; added to which attention must be paid to diet, rest and other general treatment.

When there is a high degree of anæmia, such as was observed in malaria-saturated subjects in Salonika, medicinal treatment is of little use. In these cases splenectomy has been advocated, though not practised to such an extent as to enable a correct judgment to be found of its value. Although great improvement was reported by some surgeons, it hardly seemed a justifiable procedure. It certainly did not prevent subsequent relapses. Blood transfusion was performed with apparent success in Salonika; in two cases recorded 18 to 24 ounces were introduced by direct transfusion. The immediate effect was very striking, being followed by a leucocytosis and a gradual regeneration of the red cells. As far as experience has gone at present the transfusion has to be repeated two or more times at fortnightly intervals.

According to the researches of Nierenstein approximately one-tenth of the total amount of the quinine is excreted by the urine. The method of administration did not make any appreciable difference in this rate of excretion of quinine. Quinine appeared in the urine 5 minutes after administration and could be detected for the next 70 hours. The drug is for the most part excreted unchanged, and reaches a maximum concentration of 7 to 11 grains of quinine base per litre of urine. In blackwater fever a new disintegration product of quinine, showing hæmolytic properties and called hæmoquinic acid, was obtained.

The tests for presence of quinine in the urine are best made by the Mayer-Tanret method, by dissolving 1·35 grammes of mercuric chloride in 75 c.c. of water with 5 grammes of iodide of potash in 20 c.c. of water in a 100 c.c. flask; the mercuric solution should be poured into the iodide solution under agitation. When added to urine containing quinine it produces a turbidity even in a solution of 1 in 300,000.

As regards other preparations of quinine which have been tested, such as euquinine, colloidal quinine, ethyl quitenine hydrochloride, quinoidin, quinidine, hydroquinine, chinidin, hydrochinidin, cinchonin, hydrocinchonin, chinethylin and chinopropylin, none have been found so far to exert a greater influence on malaria than the salts already mentioned, though recent work by Acton throws some fresh light on this point. He brings forward evidence to show that the laevorotatory alkaloids, quinine and hydroquinine, have a specific action on the subtertian parasite, whilst the dextrorotatory alkaloid quinidine is more powerful in its action than is quinine on the benign tertian parasite; cinchonidine behaves very similarly. Both these isomerides are much less toxic to man than quinine.

At one time there appeared to be grounds for believing that arsenical preparations such as galyl, kharsivan and neoarsenobillon in ·3 to ·6 grammes intravenously had a specific action in the pernicious forms of subtertian malaria. Undoubtedly they possess certain parasite-destroying powers, but extended experience has been disappointing. They are of value in stimulating the blood-forming organs, and are consequently of use in combating the severer forms of anæmia and cachexia which follow both forms of malaria.

Quinine Poisoning.

Quinine in moderate doses usually produces a buzzing in the ears, accompanied by slight deafness; large doses are not infrequently followed by temporary loss of hearing, but there is little evidence that it can produce permanent deafness.

Contraction of the field of vision, or quinine amblyopia, is a severe complication which may occasionally lead to total blindness, as in twelve cases which were reported from Salonika in 1917. This complication is generally the result of intense quinine poisoning with large amounts of the drug; it seldom occurs after therapeutic doses. It is surprising that it was not more frequent when the very large amounts of quinine, which were occasionally given, are taken into account. For instance, Alport advised 80 grains of quinine bi-hydrochloride daily in the first week of a subtertian fever, and cites 26 cases treated for 72 days with average daily doses of 35 grains, the maximum quantity taken during the period being 3,560 grains. Phear cites a case of quinine blindness following a severe cerebral malaria after the administration of 160 grains of quinine by the intravenous and intramuscular routes. There was another similar case with permanent blindness following the administration of 135 grains in three days.

A study of all the reported cases of quinine blindness collected by Elliott reveals the most startling variations in the amount of the drug required to produce pathological phenomena in different patients. The cases of total blindness have generally followed heroic doses administered within twenty-four hours. When more gradually administered a progressive failure of sight may be the first symptom of quinine poisoning, without any cerebral disturbance. After massive doses, on the other hand, the onset is sudden, and is noted on waking up from a comatose sleep, a condition which in itself is known to be caused by quinine.

The duration of blindness may vary ; usually it begins to pass off from fourteen to twenty-four hours after stopping treatment, but it is doubtful whether complete restoration of the vision ever occurs. A contraction of the visual field is the most constant sign. Usually the pupil becomes fixed and dilated. Fundus changes consist of a pallor of the discs, extreme contraction of the veins and arteries of the retina, with a cherry-red spot at the macula and retinal œdema. The red spot at the macula is not so vivid as in embolism ; this is explained by the constriction of the choroidal vessels, which therefore do not show up so brightly.

Other symptoms are mental confusion and it may be coma. It is necessary that the clinician should be aware of these complications and be on his guard not to attribute them to the action of the malaria parasite and so disregard the action of quinine.

There is no evidence that a moderate anti-relapse treatment causes any permanent injury to the visual acuity of the majority. The investigations of Jamieson and Lindsay on cinchonized patients showed that long-continued treatment with quinine had the effect of slightly contracting the field of vision. Their observations tended to show, however, that no one need be deterred from giving moderate doses of 30 to 45 grains of quinine a day. The extensive use of quinine during the war brought into prominence the fact, previously well known, that certain persons are peculiarly sensitive to it. In many cases this is shown by the development of ear or eye symptoms after moderately small doses. A special form of idiosyncrasy is a tendency to develop amblyopia sometimes after 2 or 3 grains of quinine. Considering the very large amount of quinine given serious effects of the administration of this drug were fortunately very rare in Macedonia. Skin rashes of various kinds, erythema, scarlatiniform rashes, urticaria and less commonly purpura have been recorded. They are generally accompanied by rise of temperature. Violet-coloured maculæ on the chest and abdomen in malaria subjects have been attributed to the action of quinine. Two serious cases of exfoliative dermatitis have been recorded by Phear.

A transient hæmoglobinuria with a rapid development of a marked anæmia, supervening upon the administration of quinine, has been reported in certain cases, and except for the absence of pyrexia such cases are apt to simulate blackwater fever.

Treatment of Malarial Invalids.

The points which have to be considered in connection with the invaliding of men suffering from chronic malaria came into prominence in 1917, when the evacuation of invalids from Salonika by hospital ships had to be abandoned in consequence of submarine warfare. At first these cases were retained in Salonika and by December 1917, some 15,000 had accumulated there, and a scheme was introduced of transferring them at the rate of 1,000 monthly to England through Italy and France, by the line of communication established between Taranto and the Channel ports.

The scheme effected an extensive reduction in the number of carriers and removed from the expeditionary force a population which did little but circulate between hospitals and convalescent depôts with an occasional day or two of light duty. It would have been difficult to justify the retention of these chronic cases with a military force operating in a country where malaria is endemic. The diminished physical fitness, the lack of energy and initiative, the state of indifference and even apathy which accompany chronic malaria, are well-recognized conditions. They seldom improve so long as the patient remains in the infected area. Especially is this the case under the conditions of active service. Apart from individual considerations the retention of men suffering from chronic malaria forms a danger to the community. It is an elementary principle of prevention that an army operating in a malarial area should avoid the proximity of native villages with their population of gametocyte carriers, and it seems illogical to retain in much closer contact with the troops large numbers of individuals equally infective.

While it was found impossible to lay down any hard and fast rules, the following conditions were accepted in Macedonia as indicating the types of cases for whom invaliding was necessary :—

(*a*) Cases in which the attack had seriously endangered life, including all cerebral cases and the other more serious pernicious forms of malaria.

(*b*) Cases in which internal organs had been severely affected, such as suprarenal cases with pigmentation, thyroid cases with exophthalmos, cases with nephritis, jaundice or pneumonic symptoms.

(*c*) Cases of malaria in association with debilitating or organic diseases, such as pulmonary tuberculosis, even if latent, gastric or duodenal conditions hindering absorption of quinine and chronic bronchitis.

(*d*) Resistant cases, relapsing while under adequate quinine treatment, or showing frequent recurrences with short apyretic intervals, especially those cases showing a continual persistent slight evening pyrexia.

(*e*) Cases followed by serious sequelæ, persisting in spite of treatment, such as marked anæmia, debility, splenomegaly, nerve lesions, mental changes, and psychoses.

(*f*) Cases with much cardiac disturbance persisting after an adequate period of regulated exercise, " effort syndrome," or marked tachycardia.

(*g*) Cases of blackwater fever or hæmoglobinuria.

(*h*) Cases of definite quinine intolerance.

The general appearance of a patient was always a valuable guide. Age might be of importance, a positive decision being given more readily in patients under 23 or over 40 years of age. And as a counsel of perfection it would have been desirable to invalid from Macedonia every case of malignant tertian malaria.

In order to estimate the average duration of invalidism, the following table, comprising a series of 3,000 cases of malaria, has been compiled by the Medical Research Council from the admission and discharge books of military hospitals in France, Salonika, Mesopotamia, Egypt and West Africa during the years 1915 to 1918. It shows the number of days during which patients were under treatment for malaria in the different theatres of war.

Force from which derived.	No. of cases.	Total No. of days under Treatment.	Average No. of days under Treatment.
France	1,050	24,475	23·3
Salonika	600	24,810	41·3
Mesopotamia	600	10,685	17·8
Egypt	550	10,993	19·9
West Africa	200	1,898	9·5
Total	3,000	72,861	24·3

Anti-relapse treatment has probably claimed more attention than any other problem in malaria during the war, as indeed the necessity of rendering such large numbers of malaria-stricken troops once more fit for active service demanded. From large numbers of experiments made under the guidance of Sir Ronald Ross in London, Oxford and Aldershot, as well as in Salonika, it appeared that a subject who has been saturated with quinine over a period of weeks or months is less resistant to the disease when he leaves off taking it than one who has not been dosed in this manner. This is probably due to the debilitating effect of the drug. In Salonika the best results were obtained, and the fewest number of relapses recorded, by administering 30 grs. of quinine on each of two consecutive days in each week, a method which has been described as the " week-end " system. By this means the number of relapse cases was diminished from 78 to 32 per cent.

Attempts to sterilize the patient by short intensive, or longer and more moderate, cinchonization have not met with success. Of the two methods the latter appears to have been the more efficacious. The cases invalided to the United Kingdom and treated at Aldershot were given two intramuscular injections of 15 grs. each and 30 grs. by the mouth for three days, followed by 40 grs. by the mouth for three weeks. In Salonika one intensive experiment of two intramuscular injections of 20 grs. combined with oral doses of 20 grs. for 12 consecutive days was found to have no advantage over the more moderate doses.

General experience has resulted in the administering of 60 grs. weekly, until the malarial subject has been free from malaria for 60 days. This method reduces the relapses of benign tertian infections to ten per cent. of cases per month. It is best given in doses of ten grains daily for six days.

In order to render malaria-infected battalions fit for active service, special measures were instituted in France when twenty-two battalions of infantry arrived in rapid succession during the months of June and July 1918 from Salonika, and 75 to 85 per cent. of the personnel in these battalions were found infected with the malaria parasite. Within a few days of arrival in France 273 men of one battalion, for example, were admitted to hospital suffering from malaria, and had the battalion then been ordered to a forward area at least 50 per cent. would have had to be retained at the base. It was evident that these troops were unfit for arduous duties at the front, and it was consequently decided to form camps for their treatment. They were formed into two divisions and the following treatment was carried out :—

(1) *Feeding.*—The diet was liberal and supplemented by bottled stout, which could be ordered by the medical officers for any men whom they considered it would benefit.

(2) *Administration of Quinine.*—15 grains of sulphate or hydrochloride of quinine in solution were given daily for 14 successive days. Afterwards for a period of two months 10 grains were given every day for six days a week, Sundays being excepted. The quinine was given at a definite hour daily either at 11 a.m. or 2 p.m. Aperients were given as a matter of routine twice or thrice a week. If a man suffered from a relapse he was admitted into a medical unit, and on his discharge the daily dose of quinine was again commenced. While in the medical unit, he received 10 grains of quinine in solution (hydrochloride or sulphate) every four hours, until 40 grains were given in the twenty-four hours. This was continued for five days. When the patient was free from fever for two days he was discharged to his unit. During the relapse treatment he received an ounce of mistura alba every morning, before any quinine was given, and his diet consisted of milk, bovril, beef-tea, arrowroot, rice; but tea was excluded. Men who had undergone 28 days' treatment without a relapse were allowed to proceed to England on leave. They were given a supply of quinine tabloids sufficient for 14 days' treatment with definite instructions to take 10 grains a day. They were also given a post-card, already addressed to their battalion headquarters, in order to let the unit know should they be admitted to hospital while on leave. No officer or man who had been in a malaria district was allowed to escape the daily dose of quinine.

(3) *Work.*—Only four hours' work was allowed during the first stage of quinine administration. Physical exercises, squad drill, instruction in signalling, Lewis gun and recreational exercises, were considered suitable work. As the treatment progressed, the daily number of hours for work was increased, and trials were instituted to see what amount of work the men could stand without developing a relapse. Route marches, commencing with a distance of five miles without packs, increased to 8 miles, 10 miles and up to 14 miles without packs, were instituted for this purpose. Medical officers took part in these marches and reported amongst other details on the number of men falling out, the causes in each instance of

falling out, and the number of relapses on the day of the route march or following days. When a series of route marches without packs was completed, a series of marches, commencing with light packs and working up to full packs, was begun. As a supreme test the troops underwent a 14-mile route march, with field operations, and a night in the open without blankets.

(4) *Recreation.*—The men were marched to the sea, allowed to remain in the water for 10 to 15 minutes, and then marched back to camp. Inter-regimental football matches, regimental sports and concerts were the order of the day. Passes were given freely to enable the men to visit the neighbouring towns, where beer was plentiful. The regimental canteens also stocked ample supplies of French beer, which was a good diuretic and tonic, contained little alcohol, and was considered better for malarial subjects, who were taking quinine, than boiled tea of which the chief constituent was tannin.

(5) *Improving the moral of the men.*—Medical officers were instructed to impress upon the men both in conversation and in lectures that malaria was a disease of no importance when quinine was obtainable and when they were removed from the infected zone. How malaria was caused, the method of transmission, and the fact that it was not an incurable disease if they followed the line of treatment laid down, was also explained to the men. Every effort was made to remove any feeling of despondency.

This course of treatment was only possible by the sympathy and co-operation of the medical officers in charge of regiments, the general officers commanding the divisions, the battalion and company commanders, and the senior N.C.O.'s.

The results were excellent, as the average duration of treatment was ten weeks, and the two divisions were put in the forward area within three months of the commencement of treatment. At a later period reports received from the administrative medical officers of the divisions showed a complete absence of anything like a malarial relapse, and the divisions, when in the field, proved as efficient in a military sense as divisions of battalions which had never been exposed to malarial infection.

The results obtained in a comparatively malaria-free country like France are not, however, likely to be obtained by similar measures carried out in a malaria-infested country such as Macedonia.

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CHAPTER XI.

BLACKWATER FEVER.

BLACKWATER Fever, also known as hæmoglobinuric fever, melanuric fever, hæmaturic fever and endemic hæmoglobinuria, is an acute disease, commonly starting with a severe rigor, and characterized by pyrexia, bilious vomiting, jaundice, hæmoglobinuria and frequently diminution or even suppression of urine.

Before the war the chief places in the world where blackwater fever occurred were West Africa, Assam, certain parts of India, East Africa and the Solomon Islands, and to a lesser degree Demerara, the southern parts of Europe and the southern states of America.

During the war, owing to the aggregation of large numbers of troops in some of these centres of the disease, to the hardships of campaigning, the great prevalence of malaria, and the exposure of considerable bodies of unacclimatized men to unusual climatic conditions, blackwater fever took a considerable toll of men on service. More especially was this the case in East Africa and Macedonia.

In the former, although no exact figures of the incidence of the disease are as yet available, many hundreds of cases of the disease among the troops were noted. The disease principally attacked the white soldiers, though Chinese labourers employed towards the end of the campaign seemed especially liable to attack. There is no record of the disease having occurred amongst the black African troops employed. Taute states that amongst the German troops in East Africa from the beginning of the war to the end of June 1917, of all cases which died other than from wounds, 64·2 per cent. were from blackwater fever. No case of the disease was ever seen by him in a native.

With regard to Macedonia more complete figures are available. Phear states that during the year ending October 1918 136 cases of blackwater fever were reported amongst the British troops in the Salonika command. Of these cases 36 died, giving a case mortality of 26·5 per cent.

With reference to the seasonal incidence in Macedonia, he shows that 116 out of the total of 136 cases were reported during the months of December to April 1917–18 inclusive, and that the incidence reached its maximum in February, in which month 32 cases were reported. During the summer months, *i.e.*, from

June to September, no case of the disease was reported until September when nine cases occurred. He is unable to account for this prevalence of the disease in the cold months of the year, but seeing that in other parts of the world the onset of an attack is frequently determined by a previous chill it may be that during the cold period of the year, when chills are readily contracted, one would expect a greater prevalence of the disease. In the preceding year, 1916–1917, only 18 cases occurred.

Arkwright and Lepper also give particulars of 16 cases of the disease observed by them in Malta, all of these cases being in soldiers transferred there from Salonika, who developed the disease whilst in Malta during the years 1916–17. Of these sixteen cases four ended fatally.

The British were not the only troops attacked by the disease. Thus Armand-Delille records its occurrence in 1916 amongst the troops forming the French Army of the East and states that the mortality was 30 per cent.

Enemy troops were also attacked. Wiener describes four cases that came under his notice in Albania. Seyfarth gives clinical details of 11 cases of the disease in Bulgaria, of whom 8 were Bulgarians, 2 Russians and 1 Turk. In a further contribution he states that blackwater fever is common in South Eastern Bulgaria, in the coastal region of South Western Bulgaria, in and around Salonika and in Greece.

In theatres of war other than Macedonia and East Africa, cases of blackwater fever appear to have been rare. Thus Mackie, writing on diseases of Mesopotamia in 1919, makes no mention of the disease, and several medical officers who served in that area stated that they never saw a case there. In Palestine also the disease appears to have occurred but rarely, at any rate in the earlier part of the campaign, though a certain number of cases were noted after the fighting in the Jordan valley.

There is no record of blackwater fever occurring in the short campaign in Togoland. During the operations in the Cameroons seven cases with five deaths were recorded amongst admissions to the base hospital at Duala.* No information is available as to its occurrence amongst the Australian and New Zealand troops employed in expeditions to certain of the South Pacific Islands.

Ætiology.

The causation of the disease is unknown. Various theories have from time to time been put forward to explain the production of the disease. Amongst these the principal are:—

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* *See* App. F, Table III. General History of the Medical Services, Vol. I.

(1) That it is due in some way to malaria.
(2) That it is caused by a specific parasite at present unknown.
(3) That it is a manifestation of quinine poisoning.
(4) That it is due to malarial anaphylaxis.

The general trend of opinion expressed by workers in the various theatres of war seems to be that the disease is the result in some way of previous malaria, the onset frequently being precipitated by some other factor, such as chill, fatigue or the administration of quinine.

It is generally agreed by most observers that the disease is almost invariably associated with previous and commonly oft-repeated attacks of sub-tertian malaria, though in very rare instances cases have been recorded in which the patient had not previously suffered from sub-tertian malaria but from one of the other varieties of malaria. Thus Stephens records such a case in which the disease followed infection with quartan malaria.

Wiener also records four cases of which three suffered from benign tertian malaria, whilst the fourth was infected with the parasites of both benign tertian and sub-tertian.

The relation of the administration of quinine to the production of blackwater fever has been widely discussed. That quinine in itself can produce true blackwater fever is generally discredited, but that quinine can in certain cases act as the determining factor in precipitating an attack of blackwater fever in a patient, the subject of much previous malaria, is undoubted. Quinine in such cases seems to act merely as the "firing charge," much as cold, chill or fatigue may act.

The theory that the disease is a malarial anaphylaxis has a few advocates and those chiefly of the continental school of thought. Widal and Ascoti were the original exponents of this view, and Porak appears to agree with them, but their views have not met with a great amount of support from British authorities.

Morbid Anatomy.

In post-mortem examination of a fatal case of blackwater fever the most notable changes are found in the kidney, spleen and liver. Microscopically the kidneys are frequently somewhat congested and may be darker in colour than normal. On microscopic investigation it will be found that the tubules are extensively blocked with casts consisting of an amorphous-like material, frequently containing granules of "malarial" pigment, but with only an occasional red blood cell. The straight tubules especially show these changes. In the great majority of cases the renal epithelium shows very little change; occasionally there may be cloudy swelling or even fatty degeneration of the cells, but this is unusual. The cells by suitable treatment will be found to contain yellow pigment and also granules containing iron in organic combination (hæmosiderin).

The liver is sometimes large and congested and shows evidence of marked blood destruction in the deposition of yellow pigment and hæmosiderin in the parenchymatous cells. Melanin may also be present. The gall bladder is usually full of very dark inspissated bile. The spleen also is congested and shows similar evidence of blood destruction and deposition of melanin. All the tissues are more or less jaundiced and the heart is commonly somewhat pale and its walls flabby.

Symptoms.

The onset of the disease is sudden and generally accompanied by a severe rigor, the temperature rapidly rising to 103° F. or 104° F. Pain of a dull aching character is commonly complained of over the liver area, over the loins or the bladder.

The patient has an urgent desire to micturate and passes a considerable quantity of almost black urine. In mild cases the urine may be of a dark brown colour rather than black. Frequency of micturition continues, but in the absence of suitable treatment the amount passed at each act of micturition tends to get less and less till perhaps only a tablespoonful is passed at a time or complete suppression may set in.

Within a few hours of the onset of the hæmoglobinuria jaundice will occur, first noticed in the eyes and gradually deepening and involving the whole body. The jaundice is not of the light lemon colour associated with ordinary catarrhal jaundice, but the colour is darker and more bronzed.

Vomiting usually sets in within some eight or ten hours of the onset of the disease. It may be almost continuous or, if early and efficacious treatment is adopted, only occasional. The vomit is bilious. The spleen is moderately enlarged.

The temperature is commonly of a remittent character but falls to normal rapidly when, in a favourable case, the urine begins to clear.

The patient rapidly becomes exhausted and violent palpitation may ensue on the slightest exertion. The pulse becomes rapid, compressible and of low tension.

In a case of moderate severity the temperature remains high for some 36 to 48 hours whilst the passage of the black or very dark urine continues. Thereafter the patient's skin becomes moist, sweating increases, the temperature falls and the urine begins to clear, the colour with each successive micturition becoming lighter and lighter until within about 8 to 12 hours after the clearing process has begun the urine will assume its normal appearance. With the complete clearing of the urine sweating stops, the temperature is down to normal or even below it, and the patient, beyond the extreme prostration, feels fairly comfortable. The jaundice, with the clearing of the urine, lessens and usually has completely disappeared within a day or two after the urine has become normal in appearance.

Such is a brief outline of a moderately severe case. In more severe cases the urine may fail to clear for some four to five days, or after the urine has cleared and the temperature has returned to normal the fever may again occur accompanied by a recrudescence of the hæmoglobinuria and the repetition of all the accompanying symptoms. On the other hand, the urine may show no signs of clearing, the amount passed may become less and less until complete suppression occurs, vomiting becomes continuous, hiccough, a very bad sign, is persistent and the patient dies. If suppression continues for two or three days, death almost certainly ensues, though recovery from such a condition has on rare occasions been recorded.

Taute records a remarkable case in which complete anuria persisted for five days. Then the patient evacuated some 500 c.c. of bloody urine. Complete suppression then recurred for eight days, when the patient died.

It is fairly common in most cases of the disease for the temperature to rise a degree or two after the urine has cleared. This is not accompanied by a return of the blackwater and seems to be due to the efforts of the body in absorbing and assimilating some of the products of the hæmolysis.

With the defervescence of this secondary fever convalescence sets in and is generally fairly rapid, though on account of the severe anæmia it is necessary to keep the patient very quiet and lying down for some two weeks or so.

Examination of the blood at the onset of the attack frequently reveals the presence of malarial parasites therein, though commonly in scanty numbers. These are usually of the sub-tertian variety, though occasionally benign tertian or even quartan may be found. With the full establishment of the attack, parasites usually disappear even without any quinine being administered. This is probably due to the destruction of the corpuscles containing the parasites by the acute hæmolytic process. Possibly such corpuscles are more vulnerable to the hæmolytic process than those not containing parasites.

Examination of the blood some hours after the attack of blackwater has commenced will reveal very grave changes. It will be seen that an extensive and massive hæmolysis has taken place, resulting in a very large diminution in the total number of red cells in the blood and a great reduction in the hæmoglobin. Instead of a normal 5,000,000 red cells per c.mm., the number will probably be reduced to 2,500,000, and with the progress of the disease this figure may fall to 1,000,000 or even less. The hæmoglobin is correspondingly diminished. No marked reduction in the number of white cells appears to take place, but a differential count reveals a relative increase in the proportion of the large mononuclears.

If a sample of the typical black urine of an ordinarily severe case of the disease be examined it will be found on standing to separate into two layers, an upper clear black portion and a lower somewhat brownish-black layer consisting of a sediment. Examination of this sediment shows it to consist largely of a granular material, together with renal casts of a somewhat amorphous character, detached epithelium and possibly a very occasional red blood corpuscle.

The urine is highly albuminous and if heated an almost solid brownish-black coagulum is produced. The albumen in the urine will persist for several days in gradually diminishing quantity, even after the urine has become clear and of normal appearance.

Spectroscopic examination of an ordinary blackwater urine shows the absorption bands of oxy-hæmoglobin, but in mild cases, in which the urine is only dark brown, methæmoglobin alone may be present. Such a mild attack may, however, be followed by a serious relapse and the passage of black urine.

The amount of dilution necessary to render any sample of blackwater urine transparent is a rough guide to the severity of the attack. Thus, if only an equal quantity of water is necessary, the attack is a mild one, whilst if two, three, four or more times the amount of water is necessary, such amounts point to progressively more severe forms of the disease. It may be difficult in the very mild forms of the disease in which only methæmoglobin is present to distinguish between such a urine and a urine darkened by bile pigment. Shaking of such a urine gives valuable information. If the colour is due to bile the froth will be of a yellowish-green colour, if to methæmoglobin of a rose-red colour.

Complications of the disease are not common. Several observers have recorded the passage of hæmoglobin or blood per anum, but the condition seems to be a rare one.

Vinson records one case of blackwater fever complicated with cerebral malaria, the blood showing sub-tertian parasites. This patient recovered.

Newham also had a similar case under his care in the East African campaign. A patient developed a typical severe attack of blackwater fever with quantities of sub-tertian parasites in his blood. Within six hours of the onset of the blackwater he became comatose. Vigorous administrations of quinine banished the coma in about 12 hours from its onset, but the blackwater persisted and the patient died the following day.

Newham has also seen one case in which typical blackwater fever was followed by a definite attack of enteric fever.

Sequelæ of blackwater fever are rare. There is always a certain amount of exhaustion and anæmia after the attack, and complete recovery may be somewhat protracted. Some authorities have noted nephritis as a rare sequel.

Patients who have once had an attack of the disease are thereby rendered more prone to subsequent attacks, and instances are on record in which patients have successfully passed through as many as ten or more attacks. The mortality seems to vary considerably, being very high in some series of cases and very low in others. Thus Plehn gives a mortality of only 4 per cent. in a series of cases seen by him, whilst other workers have recorded figures as high as 50 per cent.

During the war, although definite figures are not yet available, probably a percentage of 25 to 30 represents the mortality rate amongst British soldiers suffering from the disease. The figure under service conditions will probably be higher than under civil conditions owing to the exposure, great fatigue, repeated malarial attacks, and in many cases to the difficulty of treating such cases in unsatisfactory surroundings incidental to active service.

It is a well-recognised fact that where the necessity for moving a patient suffering from blackwater fever arises, such removal, especially after the disease has lasted ten hours, tends greatly to lessen his chance of recovery.

Prognosis.

During the course of the disease signs which are of bad omen are particularly persistent vomiting, persistent hiccough, marked diminution in the volume of the urine passed, persistence of the black urine after the third day, clouded mind and great restlessness, persistent high temperature and suppression of urine.

Diagnosis.

The diagnosis of the disease presents few difficulties. The sudden onset of copious hæmoglobinuria together with a severe rigor and rapid rise of temperature presents a picture that is not simulated by any other disease. Hæmoglobinuria may occur in a few other conditions, such as paroxysmal hæmoglobinuria and Raynaud's disease and after taking certain drugs, but the differentiation of these should present no difficulties. Difficulty may arise in very mild cases in which methæmoglobin only is passed, but the spectroscope should remove any doubts.

Treatment.

In the treatment of the disease absolute rest in bed and good nursing are imperative. The patient must be kept flat on his back and on no account allowed to sit up, and this measure should be enforced for at least a fortnight after the urine has cleared and the patient is apparently recovering, since during that period there is a grave risk of sudden fatal syncope consequent on the severe anæmia. If it can possibly be avoided it is better not to move a blackwater patient from the place where he was taken ill, and if removal is absolutely necessary it should be for as short a distance as possible and be carried out in the first few hours following the onset of the disease.

Drugs in general seem of very little material benefit in this disease. The great essential is to keep the kidneys well flushed and so to dilute the albuminous material excreted through these organs that coagulation with the formation of casts and blocking of the tubules may be prevented. The best flushing material is undoubtedly water. It may be administered in several forms and in several ways. During the early stage of the disease, when vomiting has not occurred, or is only occasional, water is best administered by the mouth, four ounces being given every hour with instructions that it should be sipped at intervals and not all swallowed at one time. The water may be given in the form of soda water, barley water, milk and soda, or any other form in which it is acceptable. Should vomiting become so frequent that the stomach cannot retain the water, recourse must be had to some other form of administration. Perhaps the best method is to introduce into the rectum every hour six ounces of normal saline, suitably warmed. If care be taken to introduce it slowly and a larger bulk than six ounces is not administered at one time irritation of the lower bowel is not produced and repeated injections can be given. Other methods of introducing water into the system are by means of subcutaneous or intravenous injections of saline, one to two pints being injected on each occasion.

In whatever way fluid is supplied care should be taken to measure accurately the amounts of urine passed, as by so doing any diminution in the output of urine is soon detected and measures can be taken to increase the intake of fluids. Generally speaking, an excretion at the rate of about four ounces per hour should be aimed at.

Stimulating diuretics should not be employed as there is a danger of over-stimulation of the kidneys and failure of excretion. The administration of fluids should be continued until the urine is quite clear.

The patient should be kept warm and guarded from chills, and he is best kept in blankets which should be changed as often as marked sweating occurs. Tepid sponging after sweating is very grateful to the patient.

The advisability of administering quinine in blackwater fever, in view of its known action as a common precipitating agent of the disease, has aroused marked diversity of opinion. Some authorities recommend its use whilst others never employ it. Perhaps the safest course to adopt is to administer quinine in small doses if malarial parasites are found by the ordinary or the thick film method to be present in the blood, otherwise to withhold it. The blood should be examined by both thick and thin film methods, as parasites are often scanty and easily overlooked.

Burkitt has shown that in this disease there is a well-marked acidosis, and to combat this some authorities have recourse to intravenous injection of a one per cent. solution of sodium carbonate. Others employ Hearsey's mixture (solution of perchlor. of mercury m. 30, bicarbonate of soda gr. 10, water to one ounce). An ounce of this is administered by the mouth every three hours till the urine clears. It is doubtful whether these drugs have much influence on the course of the disease, but the employment of Hearsey's mixture seems to control somewhat the tendency to vomit. The vomiting may be relieved also by sinapisms to the pit of the stomach, sucking of ice, or by a small dose of morphia hypodermically. Hiccough is best controlled by blistering the left side of the neck over the course of the pneumogastric nerve.

Food is best withheld in the early part of the attack, but as soon as the stomach can tolerate it fluid diet in the form of milk, albumen water, Benger's food, may be administered. In some cases resort to rectal feeding may be necessary. Stimulants may be necessary, and in such cases champagne, preferably iced, is recommended.

Many drugs have been recommended from time to time as having distinctly beneficial results in this disease. Several have recommended and used salvarsan in one or other of its various forms, but a study of their results does not appear to show that cases so treated do any better than those treated on the lines recommended above. In the case of most other drugs the number of cases treated is commonly so small that no conclusive opinion as to their merits is warranted.

During convalescence, good easily digested food should be given, the bowels kept acting freely, and iron and arsenic administered as tonics.

In view of the liability to recurrence it is advisable that all patients on recovery should be evacuated from the infected area to a non-malarial country.

It cannot be too strongly emphasised that mild cases of the disease, those in which methæmoglobin only is being passed, must be treated with the same scrupulous care as the more severe cases with passage of black urine. Any neglect in such cases may lead to what in the first instance was a mild attack developing into one of a fulminating and fatal type.

Seeing that the cause of blackwater fever is unknown it is impossible to lay down exact rules as to the definite preventive measures necessary.

In view of the undoubted close association between malaria, especially sub-tertian, and blackwater fever, measures directed against malarial infection would seem to offer the best chance of success. It has been shown in various parts of the world that by successful application of methods designed to limit infection with malaria, the incidence of blackwater fever has fallen concurrently with a marked reduction in the malarial incidence. All prophylactic measures adopted for malaria would therefore seem to be indicated in the case of blackwater fever. Where prophylactic measures include the taking of quinine, it is important that prophylactic doses of quinine should be taken regularly, as many authorities hold that irregular administration of prophylactic quinine is apt to precipitate blackwater fever.

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CHAPTER XII.

TRYPANOSOMIASIS (SLEEPING SICKNESS).

TRYPANOSOMIASIS is an African disease due to the invasion of the body by a specific parasite (trypanosoma); it is characterized by a long-continued irregular fever, adenitis, a rash, rapid action of the heart, enlargement of the spleen, and, unless efficiently treated, terminates fatally by involvement of the central nervous system and the production of what is known as "sleeping sickness."

Seeing that the disease is confined to Africa, instances in British troops in the war were only found amongst men engaged in one of the African campaigns.

The incidence of the disease amongst the British was fortunately slight. So far as is known, only one case, in a naval rating, occurred in the Cameroons campaign. In the East African campaign some 20 cases in all were discovered. Of these five were Europeans, the rest being natives. Amongst the German Forces Taute records 23 cases, of which only one was in a European. This case died with a sharp attack of hæmoglobinuria. No mention is made of the fate of the 22 native cases.

Of the 20 cases amongst the British in East Africa the histories of 18 are given by Newham. The other two cases were in natives. One was an East African native whose previous history it was impossible to obtain, whilst the other was a West African native soldier. In the latter, trypanosomes were discovered in the course of ordinary routine blood examinations, but he had no symptoms pointing to trypanosomiasis. From the fact that the parasites were quickly banished from the peripheral circulation with a few doses of atoxyl it is probable that they were of a low form of virulence and that this individual contracted his infection in West Africa and not in East Africa.

Ætiology.

The causative organism of the disease is the trypanosoma. Although no distinctive morphological differences can be made out in the organisms causing the disease in various parts of Africa, it is generally held, in view of the varying virulence of the parasites and the differences in the clinical picture displayed by cases in which the infection was contracted in different parts of Africa, that probably there are several strains of the organism. Generally speaking, four types of cases can be distinguished, according to the degree of virulence :—

(1) Those in which the infection is contracted in the Belgian Congo, the French Congo and the Southern Sudan.

(2) Those in which the infection is contracted in West Africa.

(3) Those in which the infection is contracted in Uganda.

(4) Those in which the infection is contracted in Rhodesia, Nyasaland, Tanganyika Territory and Portuguese East Africa.

These four groups vary considerably in the virulence of the disease, the Congo variety being the mildest, whilst the others show an increasing virulence up to the Rhodesian variety which is the most virulent of all. The first three are due to infection with *trypanosoma gambiense,* while authorities make a separate species of the Rhodesian trypanosoma under the name of *T. rhodesiense.*

The insect vector of the parasite is the tsetse fly. Different species of the fly can subserve this function in different parts of Africa. The best known and most widely distributed species which is an efficient host of the parasite is *glossina palpalis,* though in Rhodesia and in German and Portuguese East Africa, in places known to be affected with the disease, this species is unknown, and *glossina morsitans* appears to be the most important carrier. The parasite met with in German and Portuguese Africa undoubtedly belongs to the Rhodesian type.

The particular areas in these two colonies where the disease occurs have not yet been fully defined. In the former country the disease is known to exist in the northern part around the shores of Lake Victoria Nyanza, in the west on the shores of Lake Tanganyika, and in the south at several points along the River Rovuma, which forms the boundary between German East Africa and the Portuguese territory. It is of interest to note that in the campaign in East Africa it was not until the troops on both sides reached the River Rovuma, at the end of 1917, that cases of the disease began to occur.

In the case of Portuguese East Africa even less is known as to the foci of the disease. In the course of military operations in that country a long line of communications was opened up from Port Amelia on the coast towards Lake Nyasa, running almost due west from Port Amelia. At a point about 12 miles from the coast, and extending westward for about 10 miles therefrom, was a well-marked fly belt, and it was from that area that most of the cases of the disease in British troops appeared to derive their infection. One patient, however, a European officer, seemed to have contracted the infection further south in Portuguese territory, probably in the neighbourhood of the Lugenda river.

In these areas of infection *glossina pallidipes* and *glossina morsitans* were met with, the former being much the more common. *G. palpalis* was never encountered.

Morbid Anatomy.

In post-mortem examination of a case dying from sleeping sickness infection, no very gross macroscopic changes are to be seen. The spleen is usually enlarged, somewhat soft and congested, and the other abdominal organs may show a condition of general congestion. On examining the brain the pia mater is frequently somewhat dull looking, and may have a slightly obscured appearance like fine ground glass. Frequently it is more or less adherent to the brain substance, tearing the latter when attempts are made to strip it off. The convolutions of the brain may be slightly flatter than usual, and the cerebro-spinal fluid in excess of normal.

In the spinal cord no gross changes are observable. The fluid is increased in amount, and trypanosomes will usually be detected on centrifugalization.

Microscopically, sections of the brain and spinal cord show a great aggregation of small round cells surrounding the smaller blood vessels and situated between the vessel and its sheath.

Symptoms.

It is obviously very difficult to arrive at a correct estimate of the period of incubation. It has been noted by Manson that in a number of cases of the disease under his care the patients would frequently refer to some particular bite of a tsetse fly occurring shortly before the onset of the disease, which bite had been much more painful and its effects more lasting than they had ever experienced before. It has been suggested that such a bite may be the infective one and, if so, it would appear that the period of incubation varies between 5 and 21 days. Doubtless the incubation period may vary with the particular type of trypanosome introduced. In East Africa, of the Europeans who contracted the disease, two gave a very clear history of a particular tsetse bite which was extremely painful and occurred a short time before they were taken ill. In the one case a period of only five days elapsed between the bite and the onset of the symptoms; in the other 14 days. With such a virulent parasite as the Rhodesian trypanosome, the organism concerned in these cases, it may well be that the incubation period is shorter than in infection with the less virulent strains, and this seems to be borne out by animal inoculation experiments.

The chief symptoms of the disease are fever, erythema, local œdema, enlargement of the spleen, adenitis, and rapid action of the heart. The disease commonly starts with an attack of fever, usually ascribed by the patient to malaria and treated by quinine with no alleviation. At the onset of the disease there are great variations in the appearance of the temperature chart and it cannot be said that any particular type of chart is diagnostic. In the majority of cases fever comes on suddenly, the temperature rising to perhaps 103° F. or more, but rigor is rarely seen. The fever generally remains high with occasional remissions for a week or two and then tends to come down gradually.

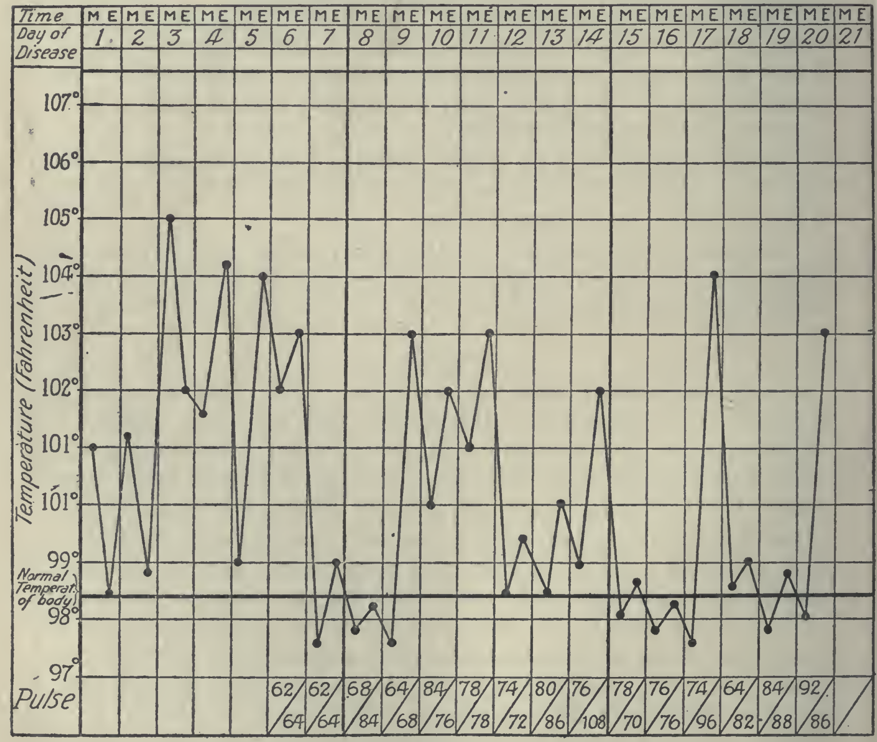

Chart I.

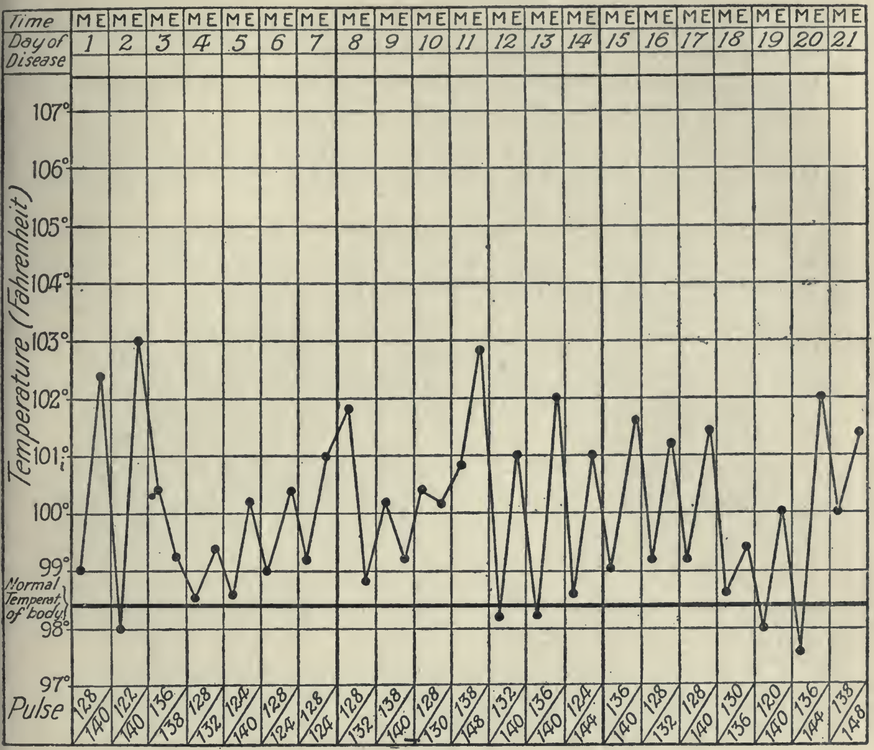

Chart II.

In other cases the fever may be definitely intermittent from the start, the evening temperature being always the higher. After about a fortnight or so what may be described as a "low" form of fever is established in which, although the temperature may not rise above 99·4° F., or thereabouts, a diurnal variation of fairly wide range is to be observed, due to the temperature falling well below normal in the apyrexial periods.

Exacerbations of the fever occur from time to time, and such are characterized by an increase in the number of parasites in the blood. (See Charts I. and II.).

The erythema associated with trypanosomiasis is most frequently seen in the early stages of the disease, but the appearance may be delayed for several weeks, and in certain cases for several months. This rash is a fugitive, patchy and usually annular erythema occurring most commonly on the chest, back and face, and less often on the limbs. The rings are usually of large size, occasionally complete, but more frequently interrupted at some point in their circumference, and the area of the skin enclosed within the ring sometimes shows discoloration resembling that seen in old bruises. The rash is extremely difficult to detect in natives, and the description given of it is based on cases in Europeans.

Local œdema is chiefly confined to the face and may affect one side, or be limited to the eyelids and those portions of the cheek just below the eyes.

Enlargement of the spleen is usually of a moderate degree, but in exceptional cases may be very marked, the organ extending to or even below the navel. The most commonly affected glands are the cervical, and especially the posterior cervical. They are enlarged, often markedly so, soft and as a rule not particularly tender. This enlargement of the glands is usually an early and fairly constant symptom in the disease. But although adenitis at some stage or other is a well-marked symptom in most cases of trypanosomiasis, it is by no means commonly present in the victims of Rhodesian trypanosomiasis. Many observers have commented upon the infrequency with which the symptom is met with in this type of the disease, and of the 20 cases in the East African campaign which came under Newham's notice only two showed this symptom and then not in a well-marked degree.

The pulse rate is commonly somewhat increased, and is readily accelerated by slight exertion, such as getting out of bed or walking across the room.

There is progressive muscular weakness so that the patient very readily becomes tired, some loss of flesh, and often a considerable degree of anæmia.

Other symptoms may be met with, but are not common. A form of hyperæsthesia known as " Kerandel's symptom " may exist, *i.e.*, if a patient strikes a limb against a hard object acute pain may be experienced out of all proportion to the strength of the blow and this production of pain is slightly delayed.

Iritis, keratitis, or retinal changes may occur and the first is occasionally one of the early symptoms. Keratitis, if it occurs, usually comes on later in the course of the disease. Optic atrophy may occur, but is in all cases probably due to over dosage with arsenic given for the cure of the disease.

Orchitis is a somewhat rare occurrence in trypanosomiasis, but occurs early and appears to be more common in infections with the Rhodesian variety of the parasite than with others.

Periostitis of the tibiæ has been noted in a few cases as occurring in the early stages of the disease.

The disease is usually prolonged, but in some cases, death supervenes early as a result of the virulence of the affection or from some intercurrent affection, such as pneumonia, to which trypanosome infected patients seem particularly vulnerable and in whom it runs a very rapid and fatal course.

On the other hand in a case not treated, or only inefficiently treated, the case may drag on for months or even one or two years and then end fatally with the symptoms of sleeping sickness. Such symptoms, marking the involvement of the central nervous system, are frequently ushered in by a slowly progressing weakness and the development of a fine tremor of the tongue and hands. Mental symptoms in the form of a rapidly developing coma, a series of epileptiform convulsions or the progressing lethargic condition known as sleeping sickness soon become manifest and the patient passes away.

In Europeans the commonest ending is in a series of epileptiform convulsions coming on suddenly and rarely lasting over 24 hours, when death occurs.

In cases that recover, beyond a particular liability to pneumonia conditions and possibly some eye trouble due to over-dosage with arsenic, there are no sequelæ of the disease.

Prognosis.

The prognosis is undoubtedly serious and has to be based on various factors. Firstly, the place where the patient was infected is an important point to be taken into account in forming an opinion, for, as has been stated, the specific organism seems to vary greatly in its virulence in different parts of Africa. If the patient has had the misfortune to become infected with the Rhodesian type of the organism the outlook is almost hopeless. So far only one case of the Rhodesian type is believed to have been cured. In cases other than the Rhodesian type the prospect is rather more hopeful, provided the patient can be removed from the infected area in the early stage of the disease and placed under thorough treatment.

The age of the patient undoubtedly has a bearing on the prognosis. It is only the younger patients who seem to tolerate well and in sufficient dosage the powerful drugs necessary to control the disease. As a rule patients beyond 30 years of age stand treatment poorly, and consequently have much less chance of recovery. Natives generally stand the treatment well, but are very apt to get tired of the prolonged medication necessary and commonly run away.

In the present stage of our knowledge it is difficult to determine when a patient is definitely cured. If he remains free from parasites in the blood for a period of a year and at the same time has had no fever or other sign of the disease he is in all probability cured, but it is advisable to prolong the treatment for a further year to be sure. Generally speaking, if, after a period of several months' freedom from parasites and symptoms, the treatment has been relaxed and parasites have then reappeared in the blood, the outlook is poor.

Diagnosis.

With regard to diagnosis, chronic irregular fever not relieved by quinine and associated with adenitis erythematous rash, and rapid heart, in a patient in Africa or who has recently resided there, should suggest the possibility of trypanosomiasis.

The actual diagnosis is determined by the finding of the causative organism. This is often scanty in the peripheral blood, and many preparations should be systematically examined before a negative diagnosis is made. The employment of the thick film method is usually of great assistance in the search for the parasite.

When failure to detect the parasites in the peripheral blood occurs it is sometimes possible to find them in the enlarged glands. The gland is punctured with a fine needle attached to a syringe and a little of the gland juice aspirated. This is blown out on to a slide, and spread out like a blood film and stained.

Failing discovery of the parasite by blood or lymph examinations, recourse must be had to animal inoculation, 10 to 20 c.c. of blood drawn from a vein being used for that purpose. The best experimental animal is a monkey, and if the inoculated blood contains parasites the animal should usually show them in fair numbers in its peripheral blood in two to three weeks.

Treatment.

Treatment, to be successful, should be commenced as early in the disease as possible. Once the patient has passed into the terminal or sleeping-sickness stage treatment of any kind is hopeless. A multiplicity of drugs have been employed for the treatment of this disease in man, but only two appear to be of any real value, namely, arsenic and antimony.

In some infections the disease seems to be well controlled and even cured by the use of arsenic only, whereas in other cases arsenic in doses short of producing serious arsenical poisoning appears to be quite ineffective. Especially is this so in the Rhodesian type of the disease. In the vast majority of cases a favourable result is to be anticipated only by the use of both arsenic and antimony. Of the various preparations of arsenic the most successful is atoxyl. This, at the onset of the treatment, should be administered thrice weekly in doses of 2½–3 grs. Later, when the disease is well under control, it may be found advisable to give it only twice weekly. Care should be taken to look out for any signs of intolerance of the drug in the shape of colic, cramps, or pains in the eyes, but as a rule with the dosage advised no ill effects are to be anticipated. Large doses, such as have been recommended by some authorities, are distinctly dangerous and liable to produce optic atrophy with total and permanent blindness. The drug is best administered by the intramuscular method deep into the gluteal muscles.

Antimony is used mainly in the form of tartar emetic. This is administered well diluted and by the intravenous method. An ordinary funnel, rubber tubing and hollow needle as used for salvarsan injections are employed. Some two to three ounces of normal saline are first introduced to make sure that everything is working well and that the needle is well in the vein. Then the appropriate dose of tartar emetic dissolved in two ounces of normal saline is introduced in the same way and followed by a further two to three ounces of normal saline to wash out the last dregs of the tartar emetic solution in the apparatus.

Certain points in the administration need attention. Care must be taken to see that none of the tartar emetic solution is allowed to escape into the tissues around the vein as a painful necrosis is set up if such an accident occurs. The tartar emetic solution and the normal saline are best made up with freshly distilled water, and all solutions must be carefully sterilized and administered at blood heat.

The reaction of the patients to such injections varies greatly. Usually, towards the completion of the injection, an attack of spasmodic coughing comes on, but passes off in ten minutes or so and is of little consequence. The temperature rises to a varying degree and is frequently accompanied by a rigor which may be very severe. The patient commonly complains of some headache. In most cases the temperature falls to normal again in three to four hours and the patient feels comparatively well. Other symptoms which may be complained of are tightness across the chest, and abdominal colic usually of a mild type, sometimes accompanied by two or three evacuations of the bowel. Vomiting rarely takes place.

With regard to the dosage of the drug it is best to start with a small dose, say, ½ gr., and to increase it by ½ gr. at each injection, until a maximum of 2½ grs. is being administered. It is found that it is impossible for some patients to take as large a dose as 2½ grs., owing to the very severe reaction produced. Such cases usually do badly and it would appear that the dose of 2½ grs. is the minimum which, if administered over a sufficient length of time, is likely to bring about a satisfactory result. The tartar emetic injections are given twice weekly.

Another method of administering antimony is to give antimony oxide in the form of subcutaneous injections of Martindale's *Injectio Antimonii Oxidi.* This may be given in one, two or three drachm doses every day. The administration is painless. The amount of antimony in the preparation is small, but appears to have a definitely beneficial effect on the disease, and is useful for supplementing other treatment.

The patient is best kept in bed during the early part of the illness and until treatment has succeeded in more or less controlling the fever and symptoms.

In a case that is doing well under intravenous antimony, it will usually be found that when no parasites are discovered in the blood, and the fever and other symptoms have abated, the reaction to the administration of the antimony becomes less and less until at the most it produces only a little discomfort in the shape of headache and possibly a rise of one degree in the temperature.

Natives appear to stand antimony much better than Europeans, and in the former repeated doses of 3, and in a few cases 3½ grs., have frequently been administered without the slightest untoward results or the causation of any particular discomfort to the patient.

The best results are undoubtedly produced by the combined atoxyl and antimony treatment, an intramuscular injection of atoxyl being given every Monday, Wednesday and Friday, and an intravenous injection of tartar emetic on the Thursday in each week, but it cannot be too strongly emphasized that, in the present state of our knowledge, treatment must be continued for a long time after all signs and symptoms of the disease have disappeared. In order to be on the safe side treatment extending over a period of two years from the time of the final disappearance of the parasite from the blood is possibly necessary before a case can confidently be proclaimed cured.

In view of the great liability to pneumonic affections to which these patients seem prone, care should be taken to instruct them to avoid the crowded buildings of theatres, cinemas and other places where they may be exposed to impure atmospheres.

General prophylactic measures against the disease, which consist in some cases of the removal of the entire population of certain areas, and the destruction of wild game over widely extended districts, are too varied and too extensive to be considered in connection with war. Personal prophylaxis consists in protecting oneself against the bites of tsetse flies. This can be accomplished by the use of veils to protect the head and neck, gloves to protect the hands, and the use of trousers and breeches, rather than shorts, so as to afford protection to the knees.

In the absence of gloves, some one or other of the fly repellant mixtures so much in vogue may be used to smear on the hands and arms. Bamber oil is probably one of the best of these, but must be frequently renewed to be effective.

White clothing is advisable as less likely to attract the fly than darker materials. Although the flies mainly bite by day, it has been shown that they will feed on moonlight nights, and, therefore, measures of protection should not be dispensed with even after sundown in a tsetse-infested neighbourhood.

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CHAPTER XIII.

RELAPSING FEVER (SPIROCHÆTOSIS).

SPIROCHÆTOSIS represents a group of acute, febrile, communicable diseases occurring in temperate, subtropical and tropical countries, and characterized by sudden onset, elevation of temperature for 24 hours or several days, rapid defervescence, and relapses occurring at fairly regular intervals of time and varying in number and severity.

So far as the war areas are concerned two distinct types must be recognized :—(*a*) the relapsing fever of Europe, Palestine, Egypt, Persia and Mesopotamia, the infection of which was conveyed by lice, with the possible exception of cases in Palestine and North Persia, where the tick *Argas persicus* may have been a vector ; (*b*) East African relapsing fever, where the infection is carried by the tick *Ornithodoros moubata*. The latter type is described separately in the chapter on East African tick fever, and the following account is concerned only with the relapsing fever of European and Asiatic theatres of war, and Egypt.

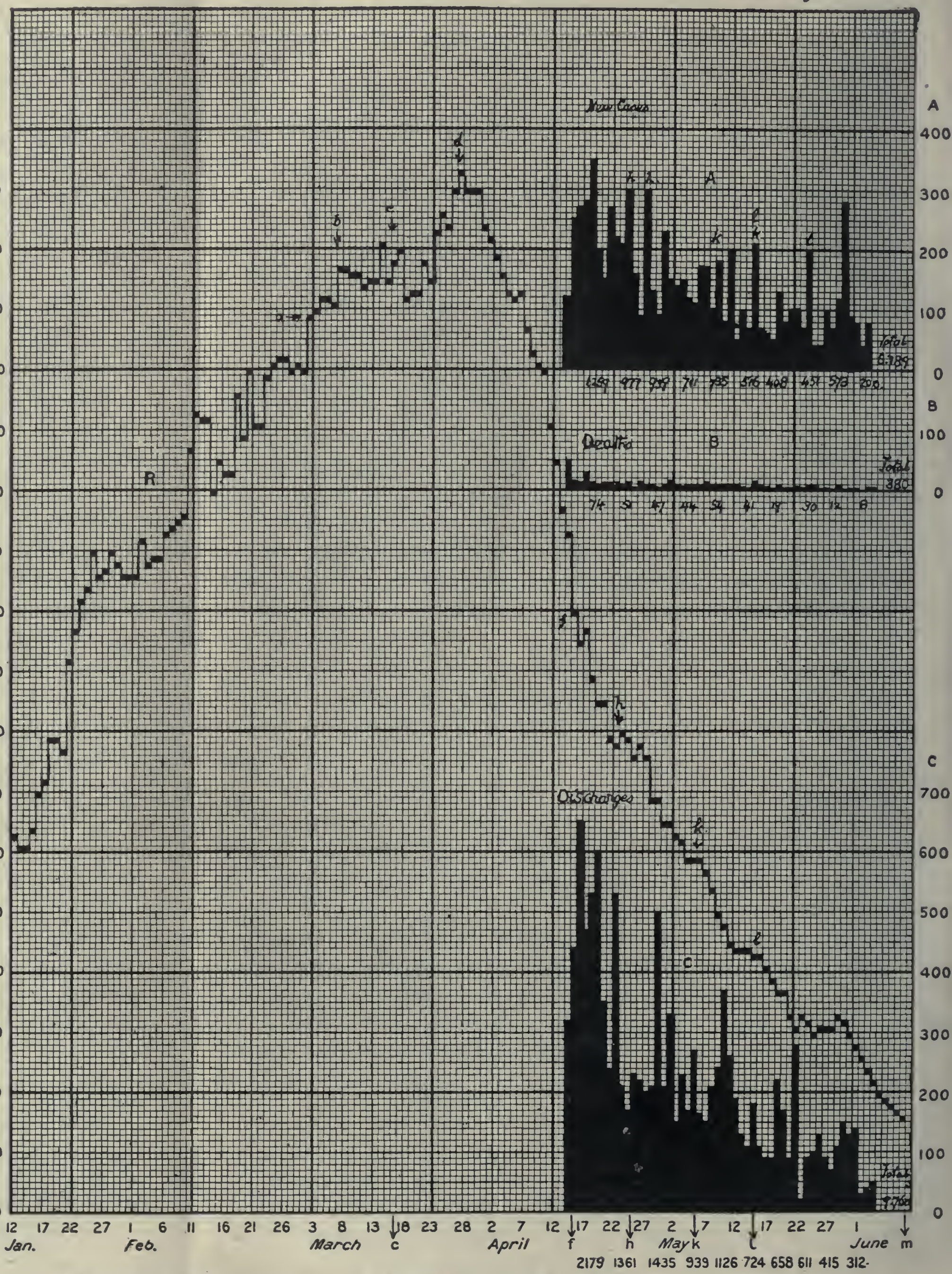
The war records show that the infection of relapsing fever, caused by lice, was not infrequently transported from place to place. Thus in 1917–18 cases were reported amongst Indian troops and Labour Corps at Marseilles, and in all probability the source of infection was Egypt. In September, 1917, a case was reported from France in one of the Chinese labourers who had reached Europe by way of Canada. Again there is evidence that the disease was introduced into Mesopotamia by the Egyptian Labour Corps, and possibly infection was also derived from India.

Mackie states that severe relapsing fever infections were brought down from Upper Mesopotamia by the Turks and that a milder outbreak at Basra was due to infection carried by a British regiment just arrived from Port Said. The Turkish troops in Mesopotamia suffered heavily throughout the whole period of the war.

Ætiology.

Ledingham has directed attention to the relation of the disease in 1917–18 to the meteorological conditions peculiar to Mesopotamia and the effect of the latter on the prevalence and

Chart I Course of Epidemic of Relapsing Fever in Serbia 1915, as shown by
R No. of Cases in Hospitals
A " " New Cases (Ap. 17–June 4)
B " " Deaths
C " " Discharges



a = *Arrival of Mission*
b = *Programme of Prevention*
c = *Suspension of Railway Traffic*
d = *Arrest in No. of Cases in Hospital 10 days after c.*
f = *Resumption of Railway Traffic*
h = *Increase of Cases in Hospital 10 days after f.*
k = *A Second increase 10 days after h.*
l = *A Third increase 10 days after k. due to evac. of F.d Ambul.*
m = *Mission left Serbia.*

activity of lice. It started from small beginnings in the last quarter of the year 1917, and attained its greatest prevalence in April 1918, falling thereafter abruptly to minimal or zero figures in the hot season. Indian troops were chiefly attacked. After April, conditions became increasingly unfavourable for the louse, the very high temperature with rapidly diminishing humidity being inimical to breeding, whilst the hot weather led to shedding of superfluous clothing and to excessive sweating, thus depriving the louse of comfortable shelter.

Very serious epidemics occurred in Serbia. That of 1915 has been fully dealt with from the epidemiological standpoint by Hunter. The chief points to which he directs attention are sufficiently indicated in Chart I.

Climatic conditions such as cold and wet, which drive men indoors and may, under certain conditions, lead to overcrowding, undoubtedly predispose to relapsing fever. Verminous soldiers, huddling together for the sake of warmth, fall victims if infected lice are present to transmit the disease. The lice-borne forms are not influenced by soil or race but if *A. persicus* is regarded as a vector the sandy soil in which this tick loves to harbour must be considered in this connexion. In former times relapsing fever was known as famine fever, and it is amongst starved and debilitated populations that the disease assumes its most virulent form and spreads with the greatest rapidity. A good example is seen in the case of Serbia. Exposure and fatigue doubtless also act as predisposing causes.

In the case of white troops close association with natives, such as those composing the Egyptian Labour Corps, or inhabiting infected villages favours the dissemination of the fever. Cases are likely to occur when men have to be transported in crowded trains and vessels and indeed under all conditions which render lice numerous and active.

If there are forms of the disease due to the fowl tick, sleeping in places infested by these vermin predisposes to infection. Certain caves, rock tombs and masonry buildings in Palestine may, therefore, be cited as sources of infection. The ticks are also often found in native wooden bedsteads. The work of Ed. Sergent and Foley in Algeria clearly shows that *A. persicus* plays no part in the case of the North African disease. In Persia a species of *Ornithodoros* is more likely to be a vector than *A. persicus* to judge from the pre-war work of Dschunkowsky.

The exciting cause is a *Spironema*, and hitherto it has been customary to describe different species in different countries. The European form of relapsing fever is attributed to *Sp.*

recurrentis (Fig. 1), the North African form to *Sp. berbera*, the Mesopotamian variety to *Sp. carteri*. It has been suggested that the cases seen in Palestine and North Persia, Miana disease, may be due to special strains, but nothing definite is known regarding this.

According to Macfie and Yorke there is no morphological distinction between the different spirochætes. Certain strains can, however, be separated by agglutination tests with their specific sera.

Lice are the vectors, both the body louse and the head louse being carriers. It is also possible that the crab louse may be a carrier. Until recently it was believed that infection is not conveyed by the bites of lice, but from their excreta or from the crushing of the insect on the skin or mucosa, the virus entering through abrasions, but a few experiments by Rocha-Lima point to the possibility of infection being transmitted by the bites of lice. Infective material may be carried by the fingers to the nose or eye. It should be noted that the spirochæte has been proved capable of passing through intact mucous membrane and the unbroken skin. Infection by these routes is, however, quite exceptional.

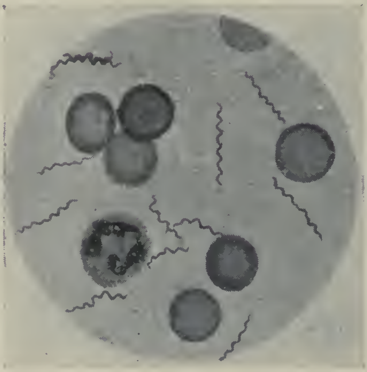


Fig. I.—*Sp. recurrentis* in human blood. (× about 1,000.)

Infection may possibly be hereditary in the louse but the evidence is conflicting. That furnished by Ed. Sergent and Foley regarding the North African spirochætosis is in favour of this being the case.

Some have incriminated bed-bugs as vectors, but it is very doubtful if they play any part in the transmission of the disease. Recent experimental work by Wiese negatives this supposition.

Morbid Anatomy.

In relapsing fever the spleen and liver are enlarged, the former being congested and often exhibiting infarcts, the latter showing cloudy swelling and sometimes fatty infiltration. Hypostatic pulmonary congestion is common. The kidneys are enlarged and congested, there are often signs of gastritis, and parenchymatous degeneration of the cardiac muscle has been noted in severe cases. In fatal cases there is usually evidence of jaundice and the bone-marrow is hyperæmic. The blood displays, as a rule, a marked polymorphonuclear leucocytosis.

Symptoms.

Apparently the incubation period may vary from a few hours to a fortnight, but, in the European form at any rate, it is usually 5 to 10 days.

The onset is very characteristic. It is remarkably sudden. The patient is taken with a chill or definite rigor, he feels giddy—an important symptom—he develops a bad frontal headache, pain in the back, joints and limbs, and he may, and often does, vomit. Implication of the calf muscles, which are often very tender, causes a difficulty in walking. Occasionally convulsions herald the attack. A feeling of heat follows. The temperature shoots up to 104° or 106° (Chart II), and the pulse grows rapid, running at 110 or 120. The patient becomes seriously ill, and is quickly prostrated and often delirious. His tongue is moist but coated with a white or yellowish fur. It is to be noted that, in contra-distinction to what is met with in typhus, the tongue continues moist throughout the illness save in very grave infections. There is constipation, the skin is usually dry and jaundice may appear, though it is often a mere conjunctival tinge. Thirst, restlessness and vomiting, it may be of blood, complete the picture, but in a minority of cases there is an evanescent rash, either rose spots like those of typhoid or a reddish mottling. Hæmorrhagic forms of the disease sometimes occur. Liver and spleen enlarge. The urine is scanty and high coloured. The appetite is poor but occasionally a voracious hunger is developed.

The patient may pass into a toxæmic state with tympanites and hiccough and eventually die, but usually, after an elevated temperature for five or six days, the first crisis takes place, and is accompanied by profuse sweating and sometimes by diarrhœa. The fall of temperature, often to subnormal, is both marked and sudden. There may be a descent of 10° F. in 24 hours. The change in the patient's condition is remarkable. His appetite returns and after a day or two he may feel so well that he is keen to get out of bed. In debilitated patients, however, the fall of temperature may be accompanied by serious collapse.

After a week or so of apyrexia the first relapse occurs. Once again the temperature swings up and all the symptoms of the first stage are repeated, sometimes in a minor degree. Sweating, however, is usually more in evidence and the amount of urine passed is increased. The temperature remains elevated for three or four days and then a second crisis occurs. The patient may

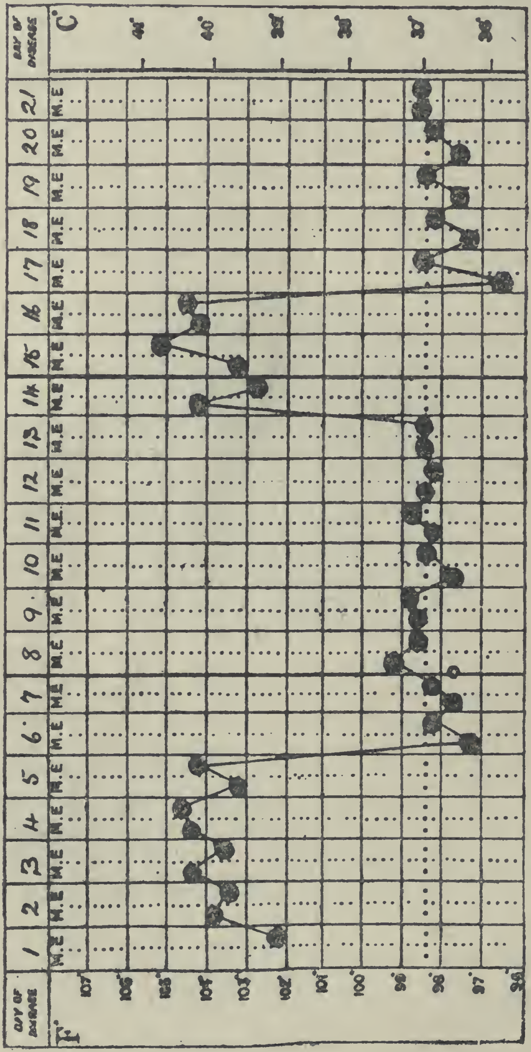


Chart II.—Typical Chart of European relapsing fever.

thereafter become convalescent or he may have a second and even a third or fourth relapse, but this is rare in the European form of relapsing fever.

The implication of the calf muscles has been mentioned, and Kuelz, who saw much of the disease in German soldiers, in Turks on the Persian front, and in Rumanians in Macedonia, Serbia and the Dobrudja, describes the resulting gait as follows: " The patient moves slowly and heavily with steps which seem to cleave to the ground . . . . he is insecure and seeks for support . . . . it is as if the trunk were too heavy for the legs." This author also states that ambulatory relapsing fever never occurs. Von Hœsslin regards hæmorrhages as characteristic, and says they occur usually just before or during the crisis and are most commonly from the nose. All his patients complained of loss of taste.

Yacoub records, in an Egyptian outbreak, four cases in which dysenteric symptoms formed the outstanding feature and this has been noted in other epidemics during the war. In one case which proved fatal no intestinal ulceration was found.

Some observers have laid stress on the presence of psychical symptoms, such as mental confusion accompanied by delirium, but in many cases acute delirium is absent, at least in the North African form, according to Parrot. Cutaneous œdema has been mentioned by several writers, but apparently does not occur in well-fed patients. It is evidence of a deficient dietary and lack of vitamines.

Castellani, recording his experiences in Serbia, directs attention to two skin features, the so-called *cutis marmorata* and flushing of the face, which he says were very frequent. Occasionally he noted a very fine rash composed of minute, roundish, delicate pinkish, or red roseola spots on the chest, abdomen and trunk.

Dudgeon, in Macedonia, found spirochætes in the urine of 27 out of 89 cases, which were specially examined for their presence, and he believes these were *Sp. recurrentis*, as they occurred along with albumin, red cells and casts, and it was noticeable that under treatment with kharsivan the condition of the urine improved.

As regards the blood, the view has hitherto been held that spirochætes are found in the peripheral circulation only during the fever periods. It is, however, possible that the introduction of the dark field and thick film methods may lead to a modification of this belief and that a few spirochætes may occasionally be found in the apyretic intervals, as indeed is the case in African tick fever. Wiener, who studied the disease in Albania in 1916–17, occasionally found spirochætes in the fever-free intervals, especially in poorly-nourished prisoners.

The polymorphonuclear leucocytosis already mentioned is associated with the febrile paroxysms. It is most marked about the critical period, but does not persist long after the crisis. It is important from a diagnostic standpoint. Boyd states that in the Palestine form there was a marked increase of large mononuclears, but, as Stitt has pointed out, this may possibly be connected with malaria or amœbiasis. According to Sterling-Okuniewski the arterial blood pressure is not altered.

Boyd separates the Egyptian from the Palestine type of relapsing fever, partly on account of the above-mentioned blood picture and partly because the spirochætes which were numerous in the Egyptian disease were scanty in the Palestine cases. Further, in the latter, the period of pyrexia was short. Mackenzie has also noted the scantiness of the spirochætes and the short duration of the pyrexial attack. As regards the latter, he says that it usually lasted from 15 to 24 hours and was represented on the temperature chart by a very characteristic spike. Another point on which he lays stress is the irregularity of the relapse, varying from seven to ten days.

Treves does not agree with Mackenzie's conclusions. Many of his Egyptian cases showed the characteristics which Mackenzie looks upon as being peculiar to the Palestine form.

In protracted cases convalescence is slow, but as a rule it is fairly rapid and recovery is complete.

Jaundice, severe diarrhœa, epistaxis, hæmatemesis and hæmaturia, parotitis, herpes labialis, nephritis, pneumonia, meningeal irritation and ophthalmia may be mentioned as complications of the disease. Tausig and Jurinac have recorded a case of spontaneous rupture of the spleen in relapsing fever, while Rudelle found various surgical complications in a Rumanian epidemic during the winter of 1916–7. He mentions cellulitis, glandular complications, myositis, osteo-periosteal and articular trouble and implication of the special sense organs such as otitis, palpebral abscess, and laryngitis.

Prognosis.

Epidemics vary greatly in intensity. In time of war amongst starved and debilitated communities relapsing fever tends to be a serious disease and the mortality, usually slight, may be very considerable.

Save under the conditions just mentioned prognosis is, generally speaking, good both as regards life and subsequent health. Marked jaundice is a bad sign. Death, when it occurs, is the result of toxæmia, collapse or some complication. As a rule, in untreated or improperly treated cases there is a certain amount of temporary debility, but it is rarely necessary to evacuate a convalescent. Provided he can be well fed and looked after, the period of invalidity, after all attacks have ceased, need not exceed a fortnight or three weeks. A great deal depends on prompt diagnosis, and early and appropriate treatment, as the disease can be cut short by suitable remedies. A certain immunity is acquired after one or several attacks, and it may last for some weeks or months, but is not absolute. Agglutinating and germicidal substances have been demonstrated in the blood of infected animals. Phear says that when visiting hospitals in Southern Russia, Northern Persia, and the Caucasus, he found that no treatment was considered necessary, all the patients getting well without it. This, he thinks, pointed to a relative immunity in those peoples among whom the disease was endemic.

Diagnosis.

Although in typical cases with several relapses a diagnosis can usually be made from the temperature chart, generally speaking the disease can only be diagnosed with certainty by the discovery of the specific organism in the blood. Whenever a microscope is available the diagnosis should be made at the time of the first attack. Under conditions obtaining in the field this is best done by the thick-drop method, described in the next chapter. The dark field method, when available, is of great service, and Coles has introduced a modification of it which consists in examining in a dry state a film containing spirochætes, stained in the usual way with Giemsa or Leishman's stain, with dark-ground illumination, using a dry lens of medium power. No mounting medium of any kind is employed. He considers the method simple and exceedingly valuable. Vital staining with toluidin blue solution 0·05 per cent. is useful. It is advisable to centrifugalize the urine of suspected cases and stain the deposit by the Levaditi silver method. It must, however, be remembered that spirochætes other than those of relapsing fever have been found in the urine in various maladies and also in healthy people.

During the apyrexial periods when no spirochætes can be found in the blood and in cases where spirochætes are very scanty and difficult to demonstrate, the diagnosis may be aided by Lowenthal's method if a case showing spirochætes is available. From the latter a drop of blood containing spirochætes is mixed with a drop of blood from the suspected case, sealed under a cover slip and incubated at 37° C. for half an hour. If the case is not relapsing fever most of the spirochætes remain motile, but if it is a case of relapsing fever and due to the same strain of spirochæte as the case furnishing the test drop the organisms will be found motionless and clumped. A control should always be made, the time limit being two and a half hours. For diagnosis during the apyrexial period, Aravantinos advocates splenic puncture, which he considers to be perfectly safe.

At the outset, relapsing fever may be mistaken for typhoid, typhus, trench fever, phlebotomus fever or cerebro-spinal fever but, in typical cases at least, the peculiar course of the temperature is characteristic. It should be noted that during an outbreak at Salonika previous to the war, stiffness of the neck and hyperæsthesia were prominent symptoms, the condition closely resembling cerebro-spinal fever.

Relapsing fever sometimes simulates plague and the two diseases may co-exist. This is also true of relapsing fever and typhus. Kirkovic and Alexieff have given an account of such combined infections, as have Martini and Mühlens. The pains of relapsing fever may cause it to be mistaken for acute rheumatism, but, as Von Hœsslin has pointed out, the absence of inflammation, the predominance or exclusive localization of the pain in the bones, the dry skin, the enlarged spleen and the failure of salicylates are distinguishing features.

Relapsing fever is also apt to be confounded with malaria, more especially in its later stages when a remittent or intermittent curve may be seen. In such cases the microscope must decide. It should be remembered that malarial attacks may follow relapsing fever and thereby simulate spirochætal relapses. In relapsing fever the febrile attack, unlike that of malaria, is apt to occur towards evening, while the size of the spleen varies somewhat, the enlargement being most marked during the pyrexia. Malaria and relapsing fever are not infrequently found co-existing in the same patient.

Treatment.

With regard to treatment, nursing, diet and general hygienic measures are required, as in typhus fever. After the crisis the patient is often ravenously hungry, and, if so, it is important to regulate his diet carefully, as injudicious feeding is apt to bring on bad diarrhœa and even dysenteric symptoms. Happily there is a specific which kills the parasite and cuts the disease short. This is salvarsan (kharsivan), which, as soon as the diagnosis is made, should be administered intravenously in a minimum dose of 6 grains. In the Egyptian form of relapsing fever, 9-grain doses were often found necessary and were as a rule well tolerated. Even if albuminuria is present this line of treatment is not contra-indicated. If relapse occurs the injection should be repeated. Sometimes it produces a temporary but short aggravation of the symptoms but its action is rapid and certain. According to Boyd, kharsivan was not as effective in the relapsing fever of Palestine. He thinks this may have been due to the shortness of the pyrexial period, which made it difficult to administer the drug while the spirochætes were present in the peripheral circulation. There is, however, a possibility that the strain was more resistant. Mackenzie states that salvarsan intravenously always cured the condition. In Mesopotamia, Willcox found that doses larger than 0·3 grm. were inadvisable owing to the risk of hyperpyrexia. In a limited number of cases, Boyd found that alarming symptoms followed the administration of kharsivan in as small a dose as 0·3 grm., and, therefore, in a disease seldom if ever fatal to Europeans, he questions the advisability of administering the larger dose of 0·6 grm. which was frequently given. In all probability, however, the ill effects were due to idiosyncracy or faulty technique, and from a military point of view it is certainly undesirable to withhold a specific treatment which is generally harmless and prevents a period of debility and incapacity. Ludyl or galyl may be used if salvarsan is not available. They are quite efficient in doses of from 4 to 7 grains. Foley and Vialatte report favourably on the use of neosalvarsan intravenously in North African relapsing fever. They gave doses of 0·05 to 0·1 grm. per kilo. of body weight.

Arrhenal (sodium methyl arsenate), according to Dumitresco-Mante, is also effective, but has to be given in much larger doses, namely 45 grains in 10 c.c. of distilled water. It has the advantage of being non-toxic. Like the other drugs it is administered intravenously. Wiener, however, found it useless.

Arsalyt (dimethylamino-tetramino-arsenobenzol) in half-gramme doses has been recommended both by Mühlens and Kostoff in the European form. Portocalis treated French cases at Salonika with serum collected during the first apyretic interval, and with cyanide of mercury intravenously, but the results were not encouraging.

Castellani, from his experience in the Balkans, advocates a combined therapy with salvarsan and tartar emetic. He finds that the latter prevents relapses and he usually gives it intravenously in 2 per cent. solution.

According to Daniel, iodosalyl, which consists of metallic iodine and salol in olive oil, when administered intramuscularly, is very effective. He records a hundred per cent. of cures within a month.

In debilitated persons, camphor, ammonia, digitalis or strophanthus, and stimulants are indicated. Sometimes the back and limb pains demand the exhibition of opium. If hiccough is troublesome and does not yield to the usual remedies, blistering over the line of the vagus on the left side of the neck may be tried.

The disease being lice-borne, preventive measures are the same as those for the prevention of typhus fever. But it must be remembered that the spirochæte has been found in the sweat and in the tears, and that it has proved capable of passing through intact mucous membranes and the unbroken skin. A case is on record where the disease was acquired from infected blood accidentally squirted upon the face. Dudgeon has drawn attention to the necessity of disinfecting the urine, as it may apparently contain the specific organism, and he enjoins the need of care in the transport of samples of urine in hospital.

If certain forms of the disease are proved to be tick-borne, measures very similar to those detailed under East African relapsing fever will have to be adopted.

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CHAPTER XIV.

EAST AFRICAN RELAPSING OR TICK FEVER.

TICK fever is a relapsing fever caused by the spirochæte, *Spironema duttoni*, which is transmitted from the sick to the healthy by the tick *Ornithodoros moubata.* It is commonly known as Central African relapsing fever or African tick fever and occurs over a wide area of the more tropical parts of Africa reaching from the Atlantic to the Indian Ocean, the northern limit on the west being the French Congo and on the east Uganda ; the southern limit on the west Angola, and on the east the Zambesi Valley. There is no definite evidence that the form met with on the West Coast is distinct from the East African type.

The disease was very prevalent in German East Africa, especially in places like Dar-es-Salaam and Morogoro where large numbers of black troops and carriers congregated and where the conditions were favourable for its spread. It was also apt to be acquired along the main roads and caravan routes utilized for military operations. It occurred also in British and Portuguese East Africa but statistics regarding it are very unreliable as it was constantly confused with malaria and the great majority of medical officers were not familiar with it.

Manson and Thornton have given a valuable account of the disease as seen in the Carrier Depot Hospital, Dar-es-Salaam. It is founded on observations made upon 1,500 cases during the latter part of 1917 and up to October 1918. Europeans, being less exposed to infection, did not suffer nearly as much as natives. Of the latter many different races were present and they may be grouped as West African, Central East African, Baganda (inhabitants of Uganda) and Coastal East African. A considerable proportion of West Africans in the Dar-es-Salaam area contracted the disease and in their case the infection resembled that in Europeans. Manson and Thornton argue that this lack of immunity indicates that the West Coast relapsing fever is different from the East Coast type. It should, however, be noted that the West Coast natives were Nigerians, Mendies, Hausas, Timinies and natives of Sierra Leone, who came from regions where African tick fever is unknown, for there is no record of its occurrence even so far south as the Cameroons, in which territory some of the West Coast troops had previously operated. In Central East African natives the disease, as was to be expected, appeared, generally speaking, in a somewhat modified or less severe form. In some cases the symptoms were slight probably on account of an immunity acquired from recent attacks. Cases amongst the Baganda were rare and not severe, perhaps owing to the long-standing prevalence of the disease in Uganda. The Coast Boys exhibited a marked tolerance due almost certainly to the immunity resulting from infection in early childhood.

The Belgian experience of the disease is related by Rodhain, who states—and his statement is confirmed by Van Hoof—that many of the Congolese soldiers were not immune and hence infections were numerous in Rhodesia and the districts east of Katanga. They became so frequent on the invasion of German East Africa that during the offensive of 1916 relapsing fever was one of the chief causes of sickness and mortality amongst the Belgian troops and accounted for one-sixth of the deaths. The principal centres of infection were Kigali, Bieramulo (Ussuwi), Saint-Michael, Shangugu, Kitega and Usumbara. On the high plateaux the disease was particularly severe. This was possibly due to a specially virulent type of infection but the large number of infective bites and the adverse conditions due to war and climate also played a part.

During the offensive of 1917 relapsing fever was quite a secondary cause of disease and death, as the black soldiers had learned to fear the tick and to appreciate the value of preventive measures.

Van Hoof states that infection is less severe when acquired in early life.

According to Taute, though many cases of the disease were seen amongst the German forces, it never became so prevalent as to be a real source of danger to the troops. The cases were frequently very severe and obstinate, many natives dying of collapse.

Ætiology.

The predisposing causes of the disease are intimately connected with the distribution and habits of the insect vector, which is the tick, *Ornithodoros moubata*. Thus the soil which suits the tick is also that associated with the disease. The same is true of climate but, in addition, adverse climatic conditions such as are encountered in tropical Africa predispose to infection, as do exposure, poor or deficient dietary, and fatigue. So far as race is concerned the question appears to be chiefly one of acquired immunity and hence is more individual than racial though, as noted above, certain races, owing to very general infection in childhood, are less predisposed to the disease than others.

The insect vector, *O. moubata*, is one of the Argasidæ. It is a blind tick, the general appearance of which is shown in Figs. 1 and 1A. The colour of the living tick is greenish brown and, like all the Argasidæ, it is devoid of a shield or scutum but is covered by a leathery integument. This integument is dotted over with close-set granules and exhibits several grooves both on the dorsal and ventral aspects. In gorged females these disappear. Unfed adults are about 4/10th of an inch in length, but a gorged female may be well over half an inch long and be very nearly of an equal breadth. The fecundated female after a meal of blood lays, in batches, from 50 to 100 (Manson and Thornton say 100 to 300) nearly spherical, glistening, golden-yellow eggs, the number in each batch varying. The eggs, which are agglutinated into masses, are laid in the soil or in other hiding places. They hatch in about 20 days and as the hexapod larval stage is practically suppressed it is an eight-legged nymph which emerges from the egg-shell and the larval skin.

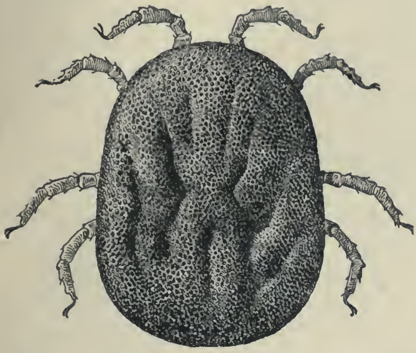

Fig. 1.—*O. moubata*, dorsal aspect (magnified).

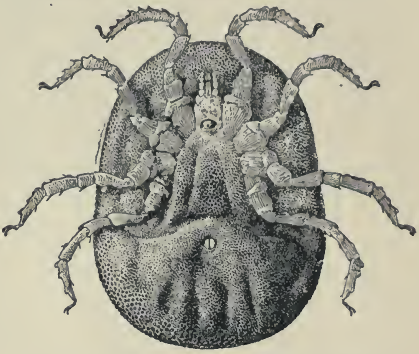

Fig. 1A.—*O. moubata*, ventral aspect.

O. moubata probably lives for several years and can survive unfed for long periods. It is very resistant to heat and germicides. It exists in native huts and in rest-houses which natives may have occupied. It may also be found under the shade of trees when the soil is dry. It is commonest along trade, travel and caravan routes. During the day it hides in the loose sand of the floors of native houses and in cracks and crannies in these floors and in the walls. Manson and Thornton failed to find the ticks in the thatched roofs of bandas in Dar-es-Salaam, but they have been described elsewhere as harbouring in thatched roofs. They are commonly found about the bases of the vertical wooden roof supports, especially when the latter are poles set in the ground, for round these poles the earth becomes somewhat loose. They are rarely, if ever, found at a greater depth than six inches. Occasionally they shelter in cracks in native wooden bedsteads. It is important to note that they may be carried long distances in packs and blankets. Both male and female ticks are blood-suckers and they sally forth on the blood quest at night. They feed both on man and animals, and as the feeding process is a slow one it can be fully carried out only when the victim is asleep. The bite is painful, may leave a tingling sensation behind it and is sometimes followed by a local inflammatory reaction.

Infection takes place as the result of the tick's infected fæces contaminating the tick-bite. One tick can infect.

The exciting cause is *Spironema duttoni*, a blood spirochæte. Its appearance is shown in Figs. 2 and 3, which are reproduced from drawings by Manson and Thornton. According to recent work by Macfie and Yorke, it does not differ morphologically from the other blood spirochætes which cause relapsing fever.

Morbid Anatomy.

With regard to the morbid anatomy of tick fever, attention may be directed to the changes in the heart found in cases dying from hyperpyrexia and indicating an acute toxæmia, there being slight dilatation and a pale, flabby and friable muscle exhibiting cloudy swelling and in certain cases fatty change. The liver in fatal cases shows acute toxic hepatitis and there is marked jaundice, the tissues being bile-stained. There seems to be little change in the spleen, save in fulminating cases, where it may become very soft and pulpy. Van Hoof records a great increase in the size of the organ in such cases. Some degree of splenomegaly is usually present in cases dying in the acute stage. The bone-marrow is hyperæmic. The kidneys may show cloudy swelling or may be almost unaffected, as in Manson and Thornton's cases.

Symptoms.

The symptoms, generally speaking, resemble those of the European form of relapsing fever, but there are certain differences, and the careful clinical observations of Manson and Thornton have added materially to our knowledge of the disease as seen during the war.

The incubation period is usually given as from two to twelve days and in many cases it would seem to be somewhere between two and seven days, shorter than is usually supposed.

The symptoms vary according to the gravity of the disease for the latter may be a mild febrile complaint, a moderately severe fever, a grave and serious pyrexia or a fulminating and rapidly fatal toxæmia. The early symptoms are lassitude, headache and vague pains.

The patient is usually irritable and dislikes being disturbed

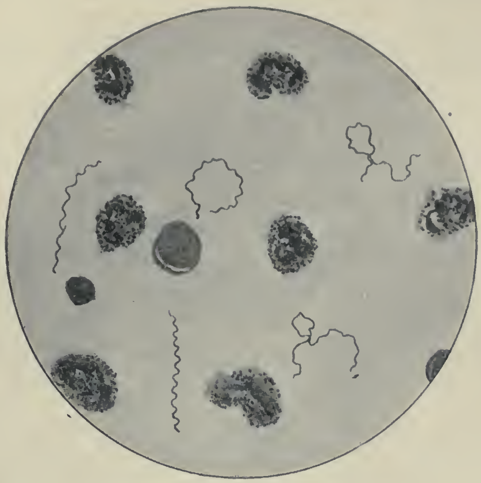

FIG. 2.—Showing an infection of moderate severity.

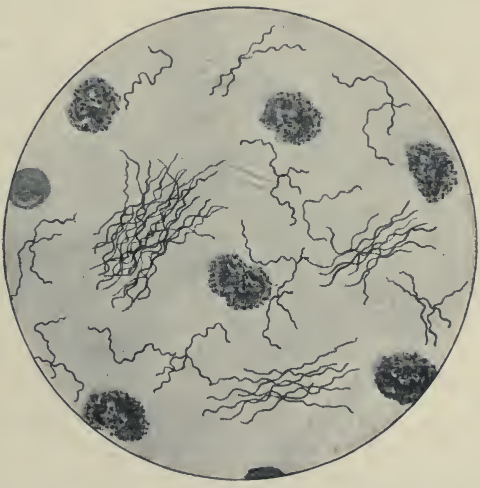

FIG. 3.—Showing masses of spirilla as met with in rare fulminating cases.

The cephalalgia is frontal, of a neuralgic nature and often very severe. There may be vomiting and giddiness at this stage. The pains are of a rheumatic type and occur chiefly in the shins and ankles. Initial rigors were rare in the East African cases but a feeling of coldness in the hands and feet and a goose-skin sensation over the surface of the trunk were not infrequent.

The course of the disease resembles generally that of European

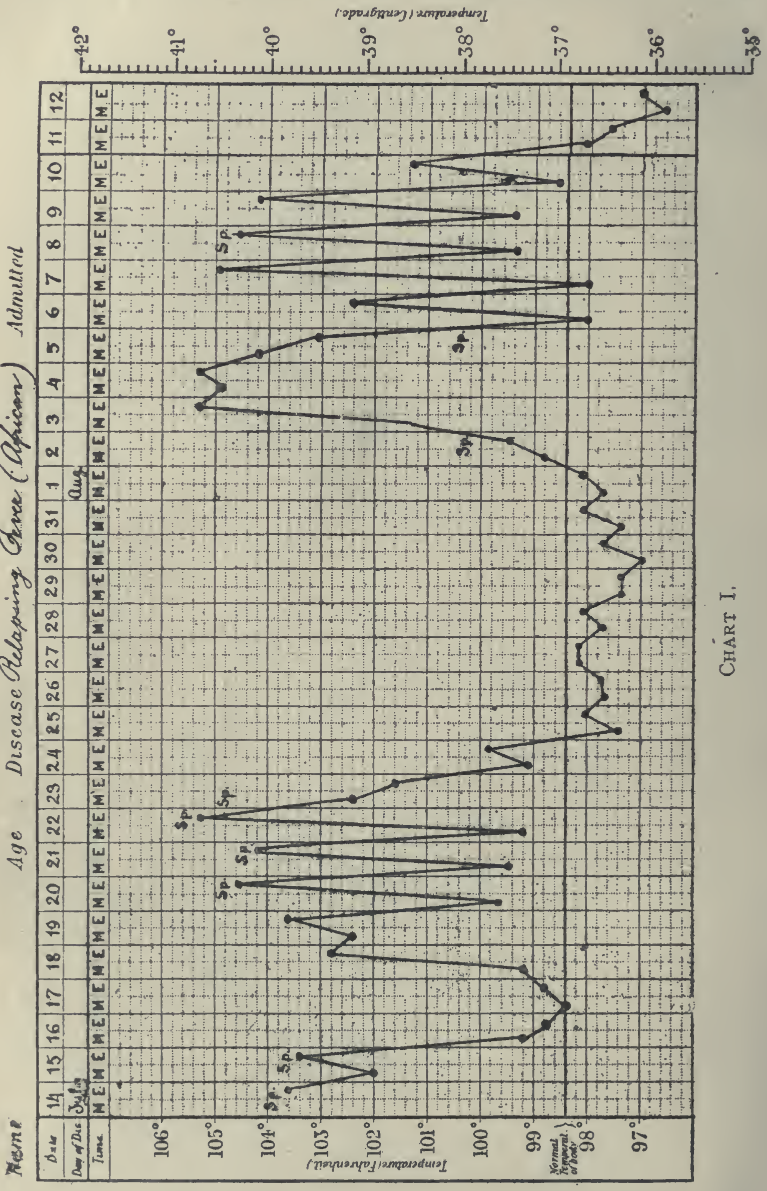

CHART I.

relapsing fever, but the initial pyrexia is usually shorter and may terminate within three days. The rise is sudden, reaches

102° to 106° F., and occurs for the most part in the latter half of the day. At first the frontal headache is severe but it passes off. Pains in the bloodshot eyes are rather characteristic but are not mentioned by Manson and Thornton. The course of the temperature is well shown in the accompanying charts. As a rule spirochætes are found in the peripheral blood chiefly when the temperature is at its maximum or when it is on the rise. This, however, is not invariably the case, for Chart I shows that they may be present during the apyrexial period, though usually only at a certain stage, that is to say, within 12 hours of the onset of the next relapse. There can be little doubt that the use of the thick-film method and dark field observations will alter existing ideas as regards the persistence of *spironemata* in the peripheral blood. The observations of Manson and Thornton, based on the thick-film method, show that the organisms are much more numerous during the first attack than in relapses, indeed in the final relapse it may be very difficult to detect them; that their number is greatest during the first few hours of the rise of temperature; and that they may be demonstrated in the blood some hours before the temperature actually rises. Contrary to general experience Manson and Thornton were frequently unable to find them during the 24 hours preceding the crisis or, if they were demonstrable, they were few in number. They were able to estimate the approximate numbers present and it would appear that in the first attack the average is about 10,000 per cubic millimetre but variations of from 500 to 50,000 were noted Very rarely there was a huge infection, the parasites equalling the red cells in number and in such cases being apparently of a special type, very long, thinner than usual and showing no tendency to looping.

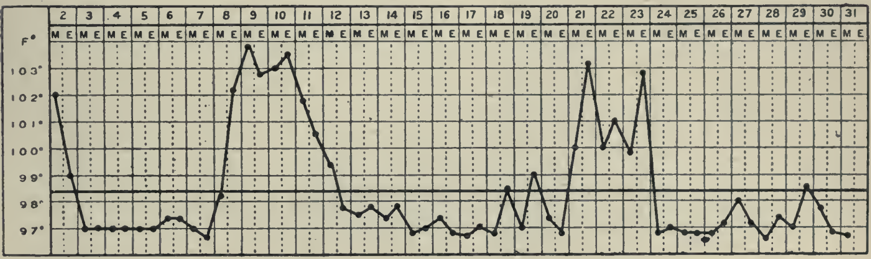

Chart II.—Saddle-back type of temperature chart.

When the temperature is not spiked but remains elevated and at a fairly constant level for a few days there is produced a saddle-back form of chart (Chart II), which is regarded as being an almost certain indication of the presence of bronchitis. In uncomplicated cases the temperature remains elevated for about a couple of days and then drops to sub-normal suddenly, usually at night. A slight pre-critical rise is sometimes in evidence. Profuse sweating accompanies the crisis and, in the case of Europeans, collapse often occurs. Manson and Thornton found collapse very uncommon in natives but Taute records it, as already mentioned. Distressing symptoms abate, the patient falls asleep and wakes refreshed and hungry.

During the attack the patient is very uncomfortable, has no appetite, has a furred tongue, an evil-smelling and foul mouth, and passes scanty and high-coloured urine which may contain a trace of albumin but there is no record of spirochætes being found in it. Diarrhœa is not infrequent and there may be dysenteric symptoms.

The apyretic intervals vary greatly in length. The first relapse appears as a rule about ten days after the initial attack but the period may be much shorter or much longer. It is usually less severe than the first attack but resembles it in its symptomatology. Sometimes the temperature is higher than at the onset, but its course is usually shorter and a sudden crisis brings it to normal or subnormal in a few hours.

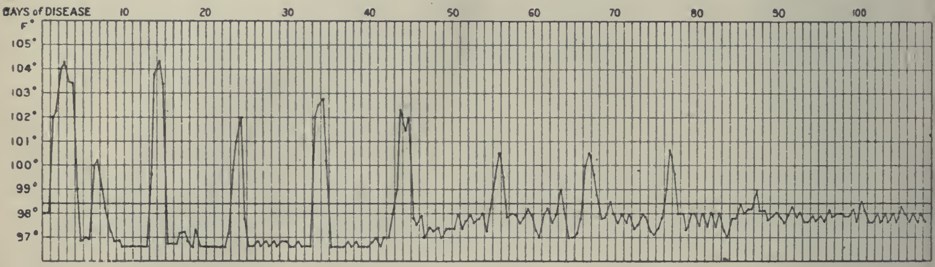

Chart III.—Typical chart of untreated case of African relapsing fever. Note nine febrile attacks and regular ten-day intervals.

A second relapse ensues after a varying interval but is less severe, and this is true of all the succeeding attacks, which may number as many as eleven, though the average would appear to be five. In cases which are untreated the tendency for each succeeding relapse to be less severe than its predecessor is evident and the last attack may be so slight as almost to pass unnoticed. As stated, the intervals between relapses vary in length but they are usually somewhere in the neighbourhood of ten days. Reford and Duke, however, record a remarkable European case in the Mwanza district, immediately south of Victoria Nyanza, in which 46 days of apyrexia intervened between the second and third relapses and 25 days between the third and fourth. During the greater part of these apyretic periods the patient was perfectly well and going about his duties. Apparently there was no question of fresh infection. In untreated cases the intervals between relapses tend to be shorter as the disease progresses. (Chart III.)

As regards the involvement of different organs it should be noted that bronchitis is common and often severe and that Manson and Thornton recognize a pseudo-pneumonic condition (Chart IV) of a remarkable nature, inasmuch as there is a sudden and complete clearing up of the physical signs at the time when consolidation may be expected to occur. Occasionally spirochætes are found in the sputum, but it is doubtful if these are *Sp. duttoni*. Save in toxæmic cases there is nothing special to note in the condition of the heart. The liver is always affected in some measure, the change being in the nature of an acute hepatitis. Jaundice is often present. The spleen is not markedly involved in uncomplicated cases. There is frequently slight splenomegaly and some tenderness over the splenic area. The kidneys do not appear to be affected. The blood, according to Manson and Thornton, shows no marked change as regards the total leucocyte and differential leucocyte count except in cases with high temperature and bronchial symptoms. These show a leucocytosis with increase of polymorphs to 75 or 80 per cent. On the other hand, Van Hoof states that there is usually an increase of basophiles, young neutrophiles and large mononuclears, and that neutrophile myelocytes and metamyelocytes are present. Polymorphs and small lymphocytes are diminished in number. The occurrence of fulminating cases has been mentioned. In these the blood swarms with spirochætes and there is an intense toxæmia causing myocarditis and grave cardiac and nervous symptoms.

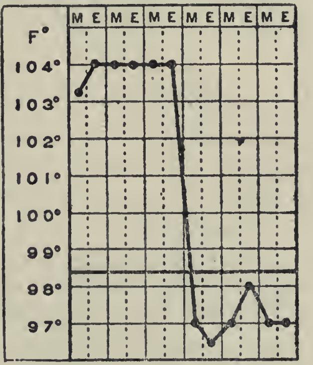

CHART IV.—Pseudo-pneumonic type of temperature.

Complications are most common in Europeans, in whom the nervous system is specially apt to suffer. Generally speaking, the complications are simple conjunctivitis and other eye affections such as amaurosis, with signs of retinitis, iritis and irido-cyclitis, very severe headaches resembling those of syphilis and yielding to mercury and arsenic, meningism, paresis of the legs, usually spastic, attacks of dysenteriform enteritis and, most important of all, myocarditis.

Manson and Thornton devote special attention to the nerve lesions seen in their cases. These occurred late in the course of the disease and were looked upon rather as sequelæ than as complications. They were of a transient nature, suggested the action of a toxin and fell into two groups: those showing gross central nervous lesions, such as aphasia, complete facial paralysis and hemiplegia; and those showing involvement of one or more cranial and spinal nerves, especially, perhaps, the third, fourth and sixth. Sometimes mixed cases occurred.

Prognosis.

The prognosis varies according to the severity of the infection and is also influenced by questions of race, immunity and facilities for nursing and treatment. Fulminant cases are fatal in a very short time. Slight cases in natives end in speedy and complete recovery. The more severe forms, both in natives and Europeans, though usually non-fatal, are very debilitating and may result in permanent damage to the heart.

Europeans, in the great majority of cases, must be invalided for a time after a sharp attack of tick fever, and will not, as a rule, recover full health and strength until they have had a thorough change and a course of tonic treatment. They should therefore be evacuated from the infected area. Natives require tonics and good food. Claims for pension may arise as a result of the nerve lesions or of permanent damage to the heart owing to myocarditis. It should be noted that Taute thinks that acquired immunity lasts only a short time, and records two cases of severe re-infection after periods of eight and nine weeks respectively.

Diagnosis.

Diagnosis can only be made with certainty by finding the spirochætes in the blood. Failing dark-field scrutiny the thick-drop method should always be employed. The procedure followed by Manson and Thornton, which, indeed, was in general use both for relapsing fever and malaria throughout the East African war area, is as follows :—

A fair-sized drop of blood is taken on the slide and spread to about the size of a shilling. It is allowed to dry for at least one hour before staining, and must be carefully protected from dust during this time. Stain with the following mixture, seeing that the whole slide is covered with stain :—

Solution 1.—Azur II, 1/1,000 in neutral distilled water.

Solution 2.—Eosin, 1/16,666. This latter is best kept as a stock 1 per cent. solution, of which three cubic centimetres are added to 500 cubic centimetres neutral distilled water. For use, mix one cubic centimetre Solution 1 with nine cubic centimetres Solution 2. This final mixture should be made up fresh daily.

This watery stain both dehæmoglobinizes and stains the film at the same time, all that remains being the stained leucocytes and any parasites that may be present lying free in the homogeneous debris of the red corpuscles. After staining for thirty minutes, flood the stain off rapidly with distilled water, and allow it to dry protected from dust.

It is highly important that the distilled water in the above be strictly neutral ; to determine this Tribondeau's hæmatoxylin test was always employed. —two drops of a saturated alcoholic solution of hæmatoxylin in a test tube half filled with water to be tested ; in neutral water, the purple colour of the hæmatoxylin will develop in between two and four minutes ; should the water be alkaline, colour is seen at once ; if acid, it is delayed. The addition of 1 per cent. acid or alkali is then made until on further testing the colour appears in the prescribed time.

The disease was most usually confounded with malaria, which can be definitely excluded only by blood examination, at least in the earlier stages. The course of the temperature serves as a guide in differentiating the two diseases, and the spleen is more frequently involved in malaria. Malaria and relapsing fever often occur together, and Manson and Thornton describe two types of cases resulting from such double infection : an irregular type, in which attacks of the two diseases bear no relationship to one another, and a regular type, in which malarial rises of temperature are seen only during the spirochætal relapse or follow immediately upon it. Naturally the former produces a puzzling form of temperature chart.

Cerebro-spinal fever and plague are other diseases which may have to be differentiated from tick fever. The importance of early and repeated blood examination cannot be too strongly insisted upon.

A point in diagnosis, not of the disease itself but in relation to it, is the technique for examining a tick to see if it is infected. This is simply done by pulling off one of its legs and examining microscopically the drop of fluid which exudes from the stump.

Treatment.

With regard to treatment, general measures and good nursing are of great importance in sharp attacks and in severe cases, for the patient suffers much discomfort, and his condition can be greatly alleviated by skilled and careful attention.

As regards the specific treatment, opinions vary and many different drugs have been tried. Probably the most reliable conclusions are those of Manson and Thornton, who carried out a series of careful tests and had ample material at their command. They recommend as a means of cure the administration of salvarsan or one of its substitutes. Of these, novarsenobillon 0·9 gramme gave the most satisfactory results in their hands. It should be given on the first attack of fever, and, failing this, on rise of temperature on the first relapse. It should always be administered on the rise of temperature, and never in the apyrexial period. Should a further relapse occur, the dose should be repeated as before on the rise of temperature. (See Charts V.–X.).

Whatever preparation be employed it is best given in concentrated form in 10 c.c. distilled water, administered with a 10 c.c. syringe. The solution must be kept at body temperature and injected at this heat, otherwise rigors are certain to follow its injection.

Van Hoof, while agreeing that salvarsan and its substitutes can cut short the disease when given early at the first febrile attack, states that in the later stages arsenical treatment can only relieve some of the symptoms and will not cure the disease. In his opinion recourse must then be had to mercury, and he recommends salicylate of mercury in doses of from 1 to 2 cg. daily, injected as an aqueous solution, to which is added a little ammonium benzoate and some drops of ammonia. Manson and Thornton, however, found the native very susceptible to the action of mercury and were unable to confirm Van Hoof's statement as to the efficacy of the drug. De Ruddere recommends "satoxyl" in the early stages. It consists of atoxyl 10 grammes, perchloride of mercury 0·3 gramme, iodide of potassium 2·5 grammes, distilled water 100 grammes. Of this 3 to 4 c.c. are given twice weekly by intravenous injection. It seems to mitigate symptoms, but is not so useful as salvarsan.

Preventive measures must be directed against the insect vector. The European usually gets infected when on the march and it is essential for him to avoid sleeping in native huts or in rest-houses which natives have occupied. He should never camp on sites previously used by natives, for these may harbour the ticks, which are able to remain without food for long periods. Native bedsteads of wood, with string or hide, are dangerous. If used, their legs should be smoothed to prevent ticks from climbing up them. It is best to employ a hammock. Sleeping on the ground favours infection. A mosquito net is useful as it prevents the access of ticks during the night, and it is

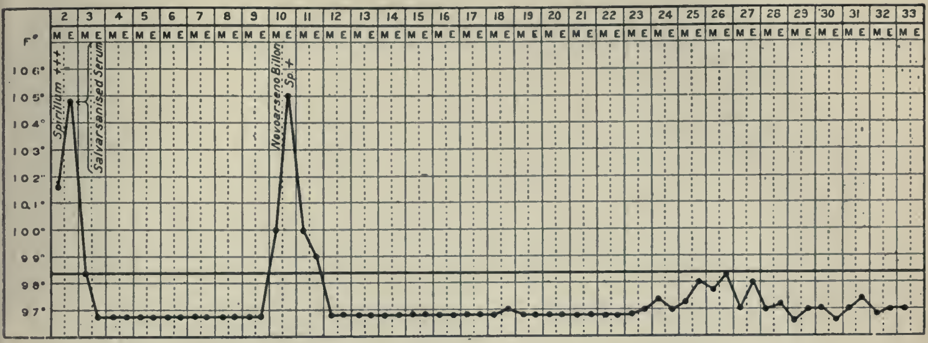

CHART V.—Treatment with salvarsanized serum showing failure; but success of novarsenobillon on subsequent relapse.

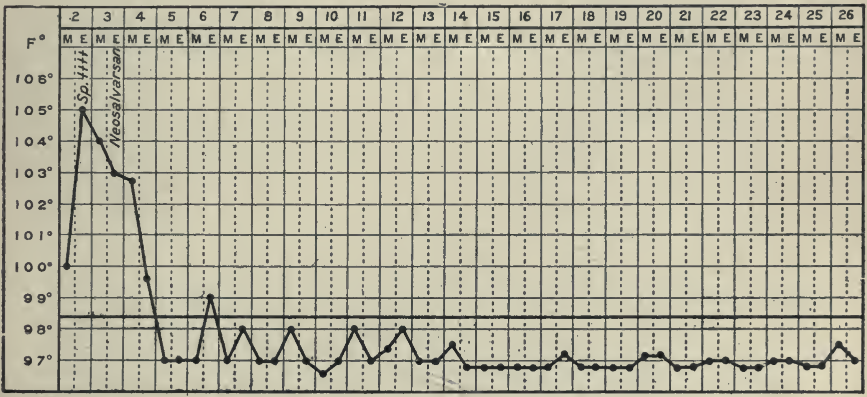

CHART VI.—Shows effect of treatment of first attack by neosalvarsan.

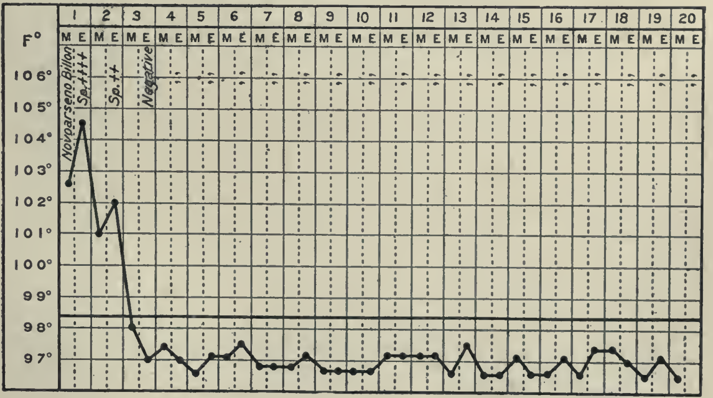

CHART VII.—First attack treated with novarsenobillon; no relapses occurred.

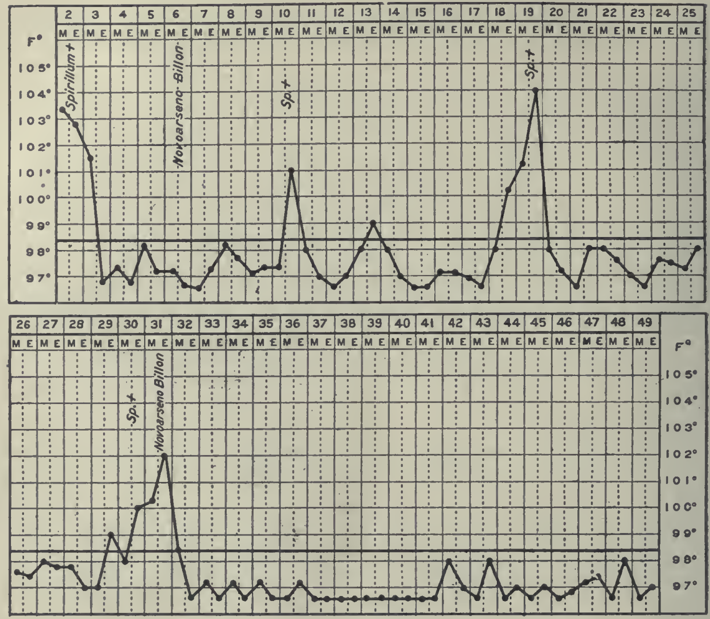

Chart VIII.—Treatment novarsenobillon in first apyrexial period, showing recurrence, but success of further novarsenobillon at subsequent relapse.

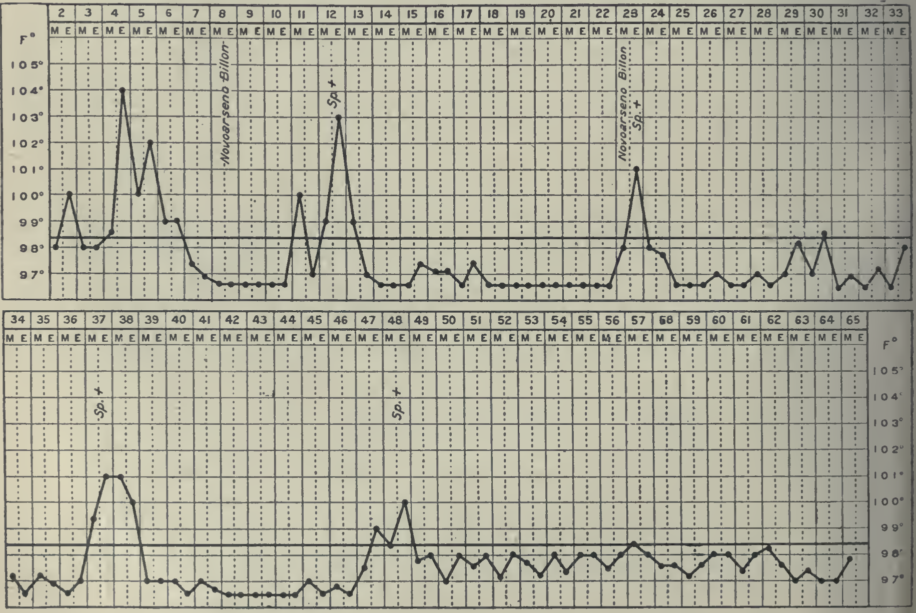

Chart IX.—Treatment novarsenobillon in first apyrexial period, showing failure; also failure of further novarsenobillon given at subsequent relapse.

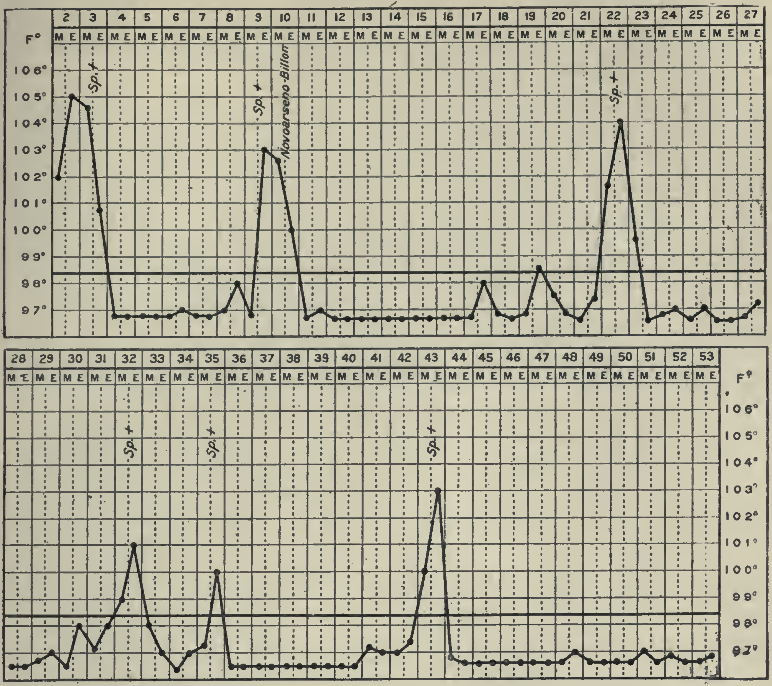

Chart X.—Treatment novarsenobillon, 0·9 gramme at second spasm of temperature.

advisable to employ a night-light, as it keeps them away. In districts known to be heavily tick-infested, blankets should be carefully inspected before beds are made up, and it is also well to institute periodical inspections of porters' packs.

Bandas should be constructed in such a way as to lessen the chances of tick infestation. For example, the reed walls of huts and bandas should be so constructed as to leave a space of eight or ten inches between the ground and the bottom of the walls. Mud and rubble buildings are to be avoided. Floors should always be raised six or eight inches and, if not of cement, hammered hard and kept clean. An excellent floor can be prepared from ant-heap earth and cow-dung, according to Manson and Thornton. The former is hammered hard on the selected site to a depth of at least four inches and allowed to set. Thereafter a top dressing of cow-dung in a liquid condition is smeared over the whole surface to a depth of half an inch. The surface is treated once a week with the watery solution of cow-dung to keep it in good order. The ticks were found to have a great antipathy to cow-dung, and a floor of this kind presents a hard, even surface which does not smell and is easily kept clean. A trench with perpendicular sides, surrounding a hut or banda, and filled with wood ash, is useful in keeping wandering ticks away.

In lines and camps, temporary buildings, which have become infested, are best burned down. The ground can be fired as it stands or the floor dug up to a depth of several inches, removed and pitted or treated with fire, care being taken that ticks do not migrate during the process. Recourse may be had to firing with the Lucal Comet Heater, or one of the other types of apparatus in which petroleum gasified under pressure is employed. Intense heat is generated, when it is passed over surfaces by means of long flexible tubes.

In permanent buildings fumigation with pyrethrum powder is indicated.

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CHAPTER XV.

PHLEBOTOMUS FEVER. (PAPPATACI, SANDFLY OR THREE-DAY FEVER.)

PHLEBOTOMUS fever is a non-fatal, acute, specific fever of short duration, caused in all probability by an ultramicroscopic organism of which the vector is a species of sandfly or phlebotomus.

It has a wide geographical distribution but, so far as the war areas are concerned, was reported from the Dardanelles, where it was especially troublesome amongst the French troops at Cape Helles during the summer of 1915, from the Ægean Islands, from Macedonia, Egypt and Palestine, and from Mesopotamia. So far as Macedonia is concerned the presence of sandflies was reported in the town of Salonika early in June 1916, and a few doubtful cases of the fever occurred during the month. In July a sharp epidemic broke out amongst the men of two mechanical transport companies camped on the Lembet Road. They had landed from Egypt four days previously. Phlebotomus flies were found in the Greek artillery barracks which they were occupying. In August of the same year the personnel of one of the field ambulances of the 22nd Division on the Doiran Front was attacked, and the fly vectors were found breeding amongst the stonework of old Turkish fountains in the vicinity. The disease was also encountered in the Struma Valley, and indeed by 1918 the whole of the Macedonian war area had been infected, the conditions at Janes and Gugunchi being especially bad.

Ætiology.

With our present knowledge any factor favouring the propagation of the sandfly must be considered as a predisposing cause of phlebotomus fever. The disease is one of sub-tropical and tropical climates, and its range probably corresponds to that of the sandfly. It may, however, be said that the fever is most common in countries which during some part of the year are very hot and dry. Thus in sub-tropical regions it occurs chiefly during the summer and early autumn. The influence of soil is only apparent in so far as the latter supplies suitable breeding places for the fly. Cotton-soil constitutes a favouring condition owing to the way it cracks, as sandflies often oviposit in the crevices. During the war the earthen parapets and sides of trenches and the walls and roofs of dug-outs, which were usually fissured, provided numerous nurseries, while crevices in caves, the interiors of rubble and stone walls, heaps of damp stones, bricks and tiles, the masonry walls of wells, old cellars, cess-pools and privies are also frequently utilized by the female phlebotomus for purposes of egg-laying. A certain amount of moisture is essential for the development of the larvæ.

Conditions aiding the transportation of the insect may possibly be considered as predisposing to the disease; hence it is well to note that the small flies may be blown considerable distances by the wind, and it has been shown that they may be carried in timber and other cargo from place to place by sea-going vessels, a matter of some importance in time of war, when hospital huts, cooking sheds, and wooden latrines are often being transported.

Little is known as regards the influence of race, but new-comers to an infected centre are specially prone to attack. War experience has shown that exposure to the sun is undoubtedly a predisposing cause, and the same is probably true as regards fatigue. It should be noted that Brack in Turkey recorded a short, febrile, epidemic illness amongst horses at the time of a phlebotomus fever outbreak. The first men attacked were those on stable guard.

The actual exciting cause is not known, but is almost certainly an ultramicroscopic organism. At any rate the work of Doerr, confirmed by Birt, Kilroy and others, points to the presence in the blood of a virus which can pass through the candle of a Pasteur Chamberland filter F, the pores of which are so fine that it arrests *Micrococcus melitensis*. Phlebotomus fever is so like dengue fever, and dengue in some respects so closely resembles yellow fever that it is possible all three diseases are due to spirochætes. If so, some special form of the parasite must be present in the blood of patients suffering from phlebotomus fever, as no spirochæte can be demonstrated by any of the ordinary methods of examination.* The virus is infective up to the end of the second day of the fever, and can be transmitted by sandflies to persons outside the infected area. A monkey has also been infected in this way. The fly does not become infective immediately after feeding on a fever case, but only

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*Couvy, in *Bull. Soc. Path. Exot.*, 13th April, 1921, says that at Beyrout a spirochæte was found in the blood during the incubation period of dengue in five or six cases, but not during the pyrexial period or after defervescence. As French writers, however, not infrequently use the term "dengue" for both dengue and phlebotomus fever, it is not quite definite which disease is referred to.

after the lapse of about a week, so that the virus must pass through some developmental cycle in the insect vector. Chalmers and O'Farrell succeeded in transmitting the disease to a monkey by the intravenous injection of infected human blood. Doerr thinks that the fly may transmit the infection to its larva, but absolute proof of hereditary transmission is lacking.

In the absence of definite knowledge as regards the causal organism the fly vector (Fig. 1) may be considered as an exciting cause. It is a moth midge or owl midge belonging to the family Psychodidæ, genus Phlebotomus, of which there are various species. *P. papatasii* is the only one definitely known to be a carrier of infection and was widely distributed during the war. It was found in Malta, the Dardanelles area, the Ægean Islands, Macedonia, Egypt, Palestine and Mesopotamia. Legendre, in the early part of July 1916, at Vignacourt near the Somme, found a packet of eggs attached to a fragment of floating manure. From these *P. papatasii* was bred out, the insect being identified by Roubaud. It has also been found near Paris. It is possible that other species may act as vectors, such as *P. minutus*, which occurs in Malta, Macedonia and Palestine, at Aden and in Mesopotamia, and *P. perniciosus*, known to exist in Malta and Macedonia and recorded by Sarrailhé from the Dardanelles.

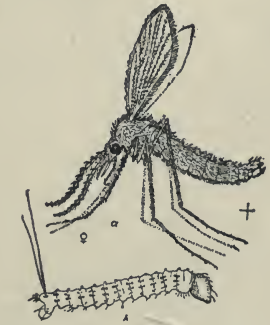

FIG. 1.—*Phlebotomus papatasii* and larva (magnified).

The fly is exceedingly minute, its tiny, hairy body, minus its legs and wings, being about a quarter the size of the head of an ordinary pin. Including wings and legs the insect occupies an area about equal to the size of a pin's head. It is therefore able to pass through the meshes of an ordinary mosquito net containing 16 to 18 holes to the linear inch. The sandfly is very delicate and of slender shape, except when gorged with blood. It has a yellowish, greyish or brownish colour. The somewhat narrow, leaf-shaped wings are large in proportion to the body, and the thin, scaled legs are of great length. Wings, body and antennæ are densely coated with short hairs, and when the fly is resting the wings project upwards from the thorax. The proboscis is as long as the head and the tips of the piercing lancets may project beyond the labium. The eyes are large and conspicuous. Sandflies dislike sunlight, but are attracted by artificial light. It is probable that they rarely traverse more than 50 yards or so in their silent flight and they do not fly high. During the day the flies shelter in the breeding places already mentioned and in hollow trees. They can also be found harbouring in the dark corners of rooms, bathrooms and latrines. The females feed chiefly at night, principally at twilight and at dawn, and are most voracious. There is no definite proof that the males suck blood. The parts chiefly attacked are the wrist and ankles and the flies will crawl under the bedclothes to get at the latter. They can easily bite through thin socks or light cotton and linen clothing. A single fly may make many punctures. After several suctions it tends to become sluggish. One fly can infect. An attack by many flies effectually prevents sleep, for the bites are painful and give rise to great local irritation. The bitten part may become much swollen and occasionally vesicles resembling those of chicken-pox may result from the punctures. In the absence of human blood sandflies will feed on animals and more especially on geckos and lizards.

P. papatasii is known to lay about 40 eggs at a time. These hatch into larvæ in from 4 to 14 days according to the prevailing air temperature. The larva is readily recognized by the long bristles, two in the young, four in the full-grown, which spring from a pair of tubercles on the last abdominal segment. The larvæ pupate in from 2 to 14 days, and the pupal stage lasts from 8 to 28 days. Roughly speaking, the complete life-cycle from egg to imago averages a month in hot weather and two months in cold. According to Birt, the winter months are passed in the larval or pupal condition. Graham, however, writing of Chitral, believes that the fly tides over this period in the egg stage.

As the disease is scarcely ever fatal, and then only from some complication, nothing is known regarding its morbid anatomy.

Symptoms.

With regard to symptoms, the usual incubation period is from four to seven days, but according to Brack may extend to 10 days. The onset is usually sudden, the attack commencing with a feeling of chilliness and malaise. There may be rigors, but these are never so severe as those of malaria. Giddiness, very severe frontal headache, pain at the back of the eyes, accentuated by pressure on the globes and the least movement of the head, pains in the back and head like those of influenza and general stiffness of the muscles soon prostrate the patient, who becomes drowsy, irritable if roused, but suffers from insomnia. The face is very flushed and may look swollen. According to Castellani this flushing may persist for from 8 to 15 days after the febrile attack and fades away very slowly. The conjunctivæ are injected so that the appearance resembles that sometimes seen in mastiffs or blood-hounds, hence the original name of the "dog disease." This eye condition, however, is by no means invariably present. Not infrequently a red line traverses the sclera, running from the cornea to the outer or inner angle of the eye. As a rule the lachrymation and catarrh seen in influenza are absent, but there may be a dry cough and a little bronchitis with some muco-purulent expectoration. Anorexia with pain or discomfort in the pit of the stomach is a feature, and constipation is the rule, though diarrhœa sometimes occurs, as does also vomiting. Amongst cases seen in Turkey, Brack observed some with dysenteric stools, cases of painful micturition, and mania. The tongue, clean at the tip and edges, is coated elsewhere by a thin white or brown fur. The fauces and palate are often congested and may exhibit small vesicles. The soft palate may present a stippled appearance due to the presence of small hyperæmic roundish spots. These do not extend to the mucous membrane of the hard palate. They are not pathognomonic of phlebotomus fever, as they may occur in relapsing fever and typhus. Epistaxis is not infrequent at a late stage in the illness. The skin is generally dry and even harsh, but may be moist. Indeed Hartley, describing an outbreak amongst Yeomanry in Mid-Egypt in 1917, states that sweating was profuse, and this has also been noted elsewhere. Apart from the face flush, which may involve the neck and upper part of the chest, there are no rashes, but these may be simulated by the numerous bites of the sandflies which, possibly as the result of scratching and irritation, may assume the appearance of a severe skin lesion, even resembling scabies. Castellani describes a delicate subcuticular mottling of the skin of the chest and abdomen—the so-called *cutis marmorata*—which seems not infrequently to be present.

The rise of temperature is rapid. By the evening of the first day's fever a temperature of 101° to 103° is reached. It seems to be highest in those who have been working in the sun. It remains elevated for about 24 hours and then begins to fall, descending gradually on the third and fourth days (Charts I–IV). In certain epidemics, however, and notably one in Macedonia, described by Delmege and Staddon, the fever in most cases terminated by crisis, the fall to normal or subnormal being very sharp (Chart V). Castellani, speaking of cases in the Balkans, says that those lasting two to three days or less terminate by crisis, while those with more prolonged pyrexia end by lysis. An after-rise of temperature is by no means uncommon in some outbreaks (Charts VI and VII).

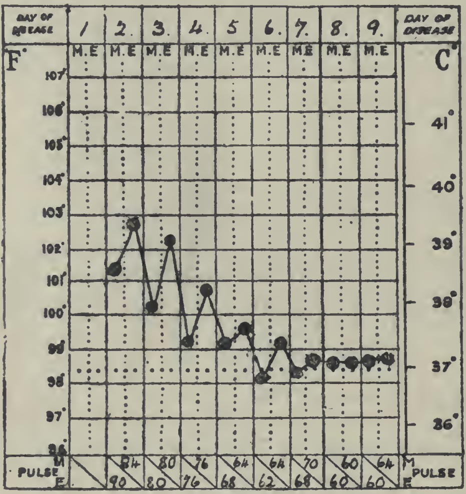

CHART I

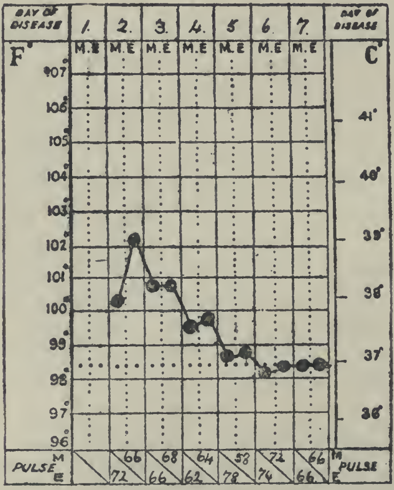

CHART II

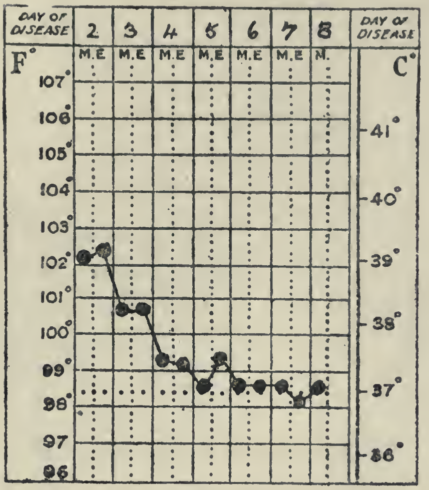

CHART III.

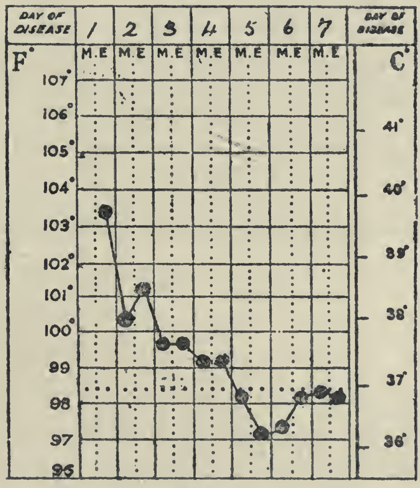

CHART IV.

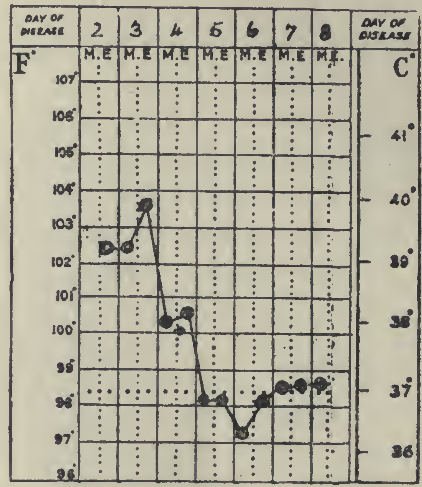

CHART V.

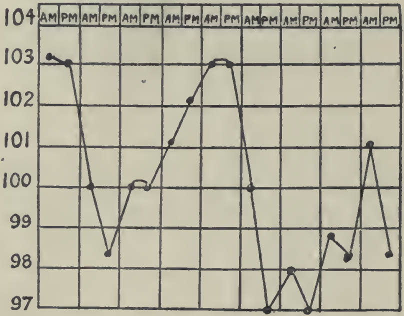

CHART VI.

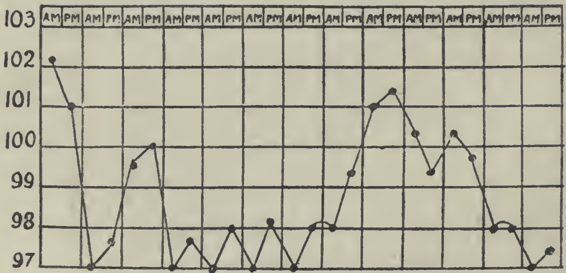

CHART VII.

The pulse rate throughout is comparatively slow, and in the later stages the pulse itself may be weak. The blood picture is rather typical, and presents a leucopenia with a relative decrease in the polymorphs. There is some increase in the large and small mononuclears. The eosinophiles diminish during the fever, but increase after it. The liver and spleen are not enlarged.

Recovery appears to be the invariable rule, and most cases of phlebotomus fever recover speedily and completely, so that invaliding need merely be of a temporary nature. In a certain proportion of cases, however, convalescence may be protracted and characterized by mental depression, loss of memory, lethargy, bone pains, neuritis, insomnia and dyspepsia. Phlebitis has been noted as a complication. General disability appears never to be permanent.

Opinions differ as regards acquired immunity. It was formerly thought that a high degree was developed, but reports of re-infection during the war were not lacking, more especially perhaps in Macedonian cases. Secondary attacks are milder than the primary ones. Re-infections must, of course, be distinguished from relapses which may possibly occur. Brack is emphatic as to there being no acquired immunity, but Adelmann, speaking of German cases in the Dardanelles, states that one attack almost always gave immunity to the soldiers.

Diagnosis.

There is no certain method of diagnosis, but in places where sandflies are present phlebotomus fever may be suspected in cases of acute fever occurring during the hot season and characterized by sudden onset, short duration, face flush, headache, injected eyes, rheumatoid pains and absence of splenomegaly. The disease must be distinguished from dengue, paratyphoid, abortive enteric fever, malaria, influenza, undulant fever, typhus, heat stroke and minor septic conditions.

Phlebotomus fever and dengue were at one time considered to be the same disease, and some still adhere to this view. The chief protagonists of this theory are Sarrailhé and Megaw. The former deals with the diseases as seen in the Mediterranean war area, and indeed speaks of a "Mediterranean Dengue" which, however, would appear to be merely a special form of phlebotomus fever exhibiting an eruption like that of dengue. Megaw draws attention to the great similarity of the two fevers in India. He states that he would subscribe to the following statement as regards phlebotomus fever :—

> "It is a disease which is either one of the modifications of dengue or is closely related to dengue. Those who consider it to be different from dengue say that it can be distinguished by the absence of a rash and by the absence of a secondary rise of temperature, though it must be admitted that in many outbreaks of undoubted dengue numbers of the cases show neither rash nor secondary fever. There is also a possibility that dengue is conveyed by a mosquito, while sandfly fever is conveyed by a phlebotomus."

Since this was written the infection of dengue has been definitely shown to be transmitted by a mosquito, *Stegomyia fasciata*, and, although there is no doubt that clinically dengue and phlebotomus fever are very much alike, it would appear advisable to regard them as distinct diseases. Seventy per cent. of cases of dengue show the characteristic rashes while in some varieties of dengue the temperature curve differs from that of sandfly fever. The conjunctival congestion seen in the latter is also rather characteristic. Castellani states that in 30 to 70 per cent. of cases of dengue the superficial lymphatic glands, especially those of the neck, are enlarged. This is occasionally seen in pappataci fever. It is conceivable that the virus of both diseases is similar, but is modified according as it passes through the phlebotomus or the mosquito.

The absence of splenomegaly serves to distinguish sandfly fever from paratyphoid, and the sudden onset is against enteric. Malaria may be distinguished by the severity of the rigor, the splenic enlargement and the presence of parasites in the blood. In influenza, catarrh is usually more pronounced, the pulse is quicker, and there is a leucocytosis and some decrease in the lymphocytes. Weinberg mentions as points of distinction the extremely rapid onset and quick rise to its maximum of phlebotomus fever, the intensity of the constitutional symptoms almost immediately prostrating the patient, the greater severity of the pains affecting particularly the ocular muscles, the greater injection of the conjunctiva and the rarity of involvement of the respiratory tract. He also draws attention to the evidence of the puncture marks of sandflies and their presence in great abundance in the locality. In Mediterranean fever the diagnosis is confirmed by the agglutination test or by blood cultures, while in typhus there is no leucopenia. In heat-stroke the temperature is higher and the nervous symptoms more pronounced. Lumbar puncture will show the cerebro-spinal fluid to be under increased tension.

Treatment.

The following table, compiled by the Medical Research Council from admission and discharge books, comprises a series of 2,000 cases treated in military hospitals in Mesopotamia and Salonika in 1916, 1917 and 1918. It shows the number of days the patients were under treatment for sandfly fever in those theatres of war.

Duration of Treatment in cases of Sandfly Fever.

Force from which derived.	No. of cases.	Total number of days under treatment.	Average number of days under treatment.
Salonika	120	1,873	15·6
Mesopotamia	1,880	21,995	11·7
Total	2,000	23,868	11·9

There is little doubt that the most valuable drug is opium, especially if given early. Its efficiency was shown in Mesopotamia and has been demonstrated in India and the Sudan. A full dose (30 drops) of liquid extract of opium administered at the outset will be found to afford great relief. Failing this, the tincture may be given, also in a full dose. Aspirin and the salicylates in fairly large doses often afford comfort, and pyramidon has been found to assuage pain. Myalgia is benefited by the application of hot sandbags. Tonics are indicated during convalescence. Quinine is useless and may aggravate the symptoms. It is advisable to apply tincture of iodine to sandfly bites. It allays irritation and lessens the risks of sepsis.

With regard to preventive measures, cases treated in infected areas in hospital should be kept under fine-mesh nets during the first forty-eight hours of fever to prevent the risk of others becoming infected. A sandfly net should have a mesh of twenty-two holes to the linear inch. Unless the material of which it is composed is very fine such a net is oppressive in a hot climate. Sandfly nets were, however, used with marked success in Macedonia, were not found too hot and, apart from the prevention of infection, enabled the men to sleep in comfort. Those living in infected areas, and especially newcomers, should use fine-mesh nets if at all possible. It is important to see that there are no flies inside the net before using it at night. They should be looked for in the angles formed by the top and sides of the net.

It has been stated that sandflies do not fly high, and Higgins, who records an outbreak of the fever from an island in the Eastern Mediterranean, found that moving men from the ground floor of a building to a lobby on the first floor was a very effective preventive measure.

Repellents smeared on the skin may be tried. Of these the vermijelli preparation containing some oil of citronella is one of the most useful. Howlett strongly recommends oil of cassia, a good formula being oil of cassia, one part; brown oil of camphor, two parts; vaseline, lanoline or salad oil, 4–5 parts. Eucalyptus oil alone or combined with the oils of anise and turpentine may be employed, a suitable prescription being :—

Ol. anisi
Ol. eucalypti } āā ♏iii
Ol. terebinth
Lanolini ʒi.
M. ft. ung.

A lump of camphor may be taken to bed, as the flies dislike its odour. Tobacco smoke keeps them away to some extent, and electric fans, especially if depending from the ceiling, are excellent deterrents. Lights in tents and bedrooms at night attract the flies. In the case of billets and houses generally, heavy furniture should stand well out from the walls, as the insects are apt to hide behind cupboards and sideboards.

Frequent cleaning, dusting and removal of hangings help to get rid of them, as do whitewashing and free ventilation.

When it can be managed camps should be placed on high-lying sites exposed to the wind and should be well away and up-wind from horse-lines. Breeding places in the neighbourhood of drinking-water fountains should be avoided after dark.

The following general measures should also be adopted. Where possible, ruined walls, masonry, heaps of rubble and stones, and old damp latrines, which harbour the larvæ, should be removed. When this cannot be done all crevices should be filled up by pointing the walls, if of stone or brick, or plastering them smoothly if of mud, as, for example, in the case of trenches and dug-outs. Where such breeding places are limited it may be possible to make advantageous use of some form of flame as, for example, a powerful painter's lamp or the Lucal Comet Heater. Rat-holes and ant-holes should be stopped. Vegetation about these places should be cleared away and kept down. Cracks in the ground, and especially in black cotton soil, should be filled up, or, if this is impossible, treated with kerosene oil. Cultivation and systematic watering prevent cracks from re-forming.

Measures should also be taken to capture the flies. For this purpose biscuit boxes blackened on the inside and placed in dark corners of the room are useful. Austen recommends that sheets of "tangle-foot" with lights in front of them should be affixed to the walls. These sheets should be slightly warmed before use. Fumigation with sulphur may be employed and spraying with 1 per cent. formalin has been recommended.

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CHAPTER XVI.

TRENCH FEVER.

TRENCH fever is an infectious disease characterized by febrile periods which tend to recur at regular intervals, by local pains, by an erythematous rash, and by enlargement of the spleen.

It was first noticed in the British troops in Flanders by Graham in the summer of 1915, in Salonika by Hurst in the latter part of the same year, in French troops in France in 1916, and about the same time in Italy. It occurred in the German and Austrian Armies, but most of the accounts given of it there, under the names of "Wolhynian fever," "five days' fever," "Polish, Russian intermittent, or Meuse fever," and "His-Werner disease," evidently confuse it with other diseases, and are not of great value as clinical records. It has also been termed "shin fever," "gaiter-pain fever," and "trench shin." It differs from any disease known to medicine before the war. Allusions to a quintan fever by ancient and mediæval writers are too vague for identification.

The name "trench fever" was first used by Hunt and Rankin. McNee, Renshaw and Brunt were the first to prove its infectious character by injection of a patient's blood into the vein of a healthy man. The clinical features of the disease were studied, and the louse was early suspected to be the vehicle, but nothing was certainly known until in 1917 the Medical Investigation Committee commenced work in France, and the War Office Trench Fever Committee in England. The American Research Committee co-operated with the former and carried out the experimental part of the work done in France, and regular communication was kept up between the groups of workers.

The disease was recognized in Flanders, France, Macedonia and Italy and in the German and Austrian Armies. It is not therefore much affected by climate or soil. All Europeans and races originally European are subject to it. It was in no army so carefully studied as in the British, but as it is easily confused with other diseases the statistical returns give no exact idea of its prevalence even in the British, still less in other armies. Age has apparently no influence. In France patients were of all ages up to 43, and in England volunteers of 70 seemed as susceptible as younger men. There was no effect traceable to food or drink. It was rightly named trench fever, for it originated in the front area, and for a long time was hardly noticed to arise at the base. Hospital officers, nurses and orderlies caught it, and later when officers and other ranks were sent from the front to army schools they brought the infection into the back areas.

It is impossible to give with any accuracy the rate of incidence among the troops. The name trench fever was not sanctioned until 1917, and the fever was not made notifiable till 1918, by which time it was much less common. In July 1918, Colonel Soltau reported that for the preceding 12 months the total admissions for all forms of sickness into the clearing stations of the Second Army were 106,247, of which

15,392	cases were diagnosed as	pyrexia of uncertain origin.
5,244	,, ,, ,, ,,	trench fever.
4,755	,, ,, ,, ,,	myalgia.
635	,, ,, ,, ,,	rheumatism.
2,535	,, ,, ,, ,,	debility.
2,587	,, ,, ,, ,,	cardiac (nearly all disordered action of the heart).

Those who could fully examine the cases received as pyrexia of uncertain origin were satisfied that the bulk of them and many also of myalgia and rheumatism were really trench fever. Without pretending to exactness, experience justifies the statement that 15,000 to 20,000 of the 26,026 cases diagnosed as P.U.O., trench fever, myalgia or rheumatism, were probably cases of trench fever. This is confirmed by the accurate observations in four base hospitals at Boulogne by Lewis, Thursfield, Jex-Blake, and Foster, who received 1,241 cases labelled pyrexia of uncertain origin, trench fever, or myalgia, and found that 822 or 66 per cent. were true trench fever. The 26,026 cases above mentioned would with the same ratio produce 17,350 cases of trench fever which would thus form 16 per cent. of the total sickness. In addition trench fever was probably responsible for a considerable number of the 5,000 chronic cases. The importance of the disease may be gathered from the following estimates. The average evacuation for sickness, as distinct from the result of wounds, from armies to base in France was 0·6 per cent. of the strength weekly. During the worst year of trench fever, 1917, the percentage figure for this disease, at, say, 15 per cent. of 0·6 per cent., would be somewhere about ·09 per cent.; that is an army of 1,000,000 would lose in a year by evacuation to the base at least 45,000 casualties from trench fever. Of these casualties, as is shown below, 80 per cent. would lose on the average 60 days in hospitals or depôts, and at least three months in all off duty; and of the remaining 9,000 more than 2,000 would be incapacitated for a period of over six months. There were no deaths, but the total loss of man-power resulting from this apparently new disease was a very heavy drain on the army.

Ætiology.

When first recognized clinically in the spring of 1915, the disease, from its general symptomatology, was suspected to belong to the enteric group of fevers, possibly modified by preventive inoculation. Much of the early work on ætiology was therefore directed to proving or disproving this theory, until evidence that the disease was a separate and complete entity was gradually collected. All cultures from the blood, stools and urine were negative, while the fact that *B. paratyphosus A* and *B* had not then been introduced into the preventive vaccine made the agglutination reactions simple in their interpretation. The experimental work of McNee, Renshaw and Brunt, showing that the blood was infective, was strongly against the enteric theory, and the proof was finally completed by the work of the American Committee.

Since the early experimental work demonstrated that the virus circulated in the peripheral blood, long search was made in blood films for a parasite, either intra or extra-corpuscular, without result. These examinations of films, moreover, did not reveal anything of diagnostic or prognostic significance for the clinical pathology of the disease. Later work has all tended to show that the virus circulating in the blood belongs to the "filter-passing" group, and is therefore ultra-microscopic. Observations on the possible nature of the virus contained in the excreta of infected lice are dealt with below. It has also been shown that the virus circulates free in the plasma during the illness.

The body louse was early suspected to be the means of transmission of the infection, and complete proof that this is the case has been afforded by the experiments of the British and American Committees. Both committees are agreed that the blood of an infected man, and the fæces of an infected louse, can be used to infect a new host, while the American workers have also shown that in some cases the urinary sediment and sputum may contain the virus. There is a point of difference in the findings of the two committees which merits attention. Whereas the American Committee hold that the disease can be transferred from man to man by the simple bite of the louse, the British Committee believe that the mere bite is insufficient, that the virus is only present in the fæces of the infected insect, and that a bite, scratch, or abrasion of any kind, is of equal importance as a point of entrance of the infection when contaminated with infected lice excreta. On this latter view Byam has brought forward evidence to show that a louse must have bitten a case of trench fever five to eight days previously before its fæces become actively infective.

In work on the fæces of infected lice, Arkwright has fully confirmed the observations of da Rocha Lima on the almost invariable presence of so-called "Rickettsia bodies" in the excreta of insects which have fed on patients suffering from trench fever. These bodies, originally found by Ricketts (1909) in the tick which transmits the disease known as Rocky Mountain spotted fever, and later by Ricketts and Wilder in the excreta from lice on cases of typhus fever, are of very small size. The following criteria are given by Arkwright, Bacot and Duncan for their recognition :—

(1) Minute size—smaller than *M. melitensis* or *B. influenzæ* —usually about 0·3 × 0·3 or 0·3 × 0·5 mm.
(2) Irregularity in shape—round, oval, diplococcal, or bacillary with stained poles.
(3) Occurrence in very large numbers, or even in masses, especially in flakes of solid material in the excreta.
(4) Well-stained appearance when coloured by Giemsa's stain, the colour being purple like that of the nucleus of a leucocyte.

These bodies appear to be in some way closely connected with the virus, but their exact relationship to the ætiology of trench fever is so far uncertain.

The remaining points of importance in the ætiology of the disease which have been clearly established concern the powers of resistance of the virus and the period of infectivity of cases of trench fever to lice, and therefore to other men.

It was established by the American Committee that the virus "resists a temperature of 60°C. moist heat for thirty minutes and is fully virulent after such treatment, but is killed by a temperature of 70°C. moist heat for thirty minutes. Obviously, therefore, a temperature of 55°C. for thirty minutes, which destroys the louse (*Pediculus humanus*) and its ova, does not suffice to destroy the virus of trench fever which may be present on the underclothing of trench fever patients."

With regard to the period of infectivity of sufferers from trench fever, Byam has published observations on chronic cases which show that the virus may still be present in the blood for a very long time after the onset. He gives two instances in which lice were infected and transmitted the disease to a new host by feeding on chronic cases who had been first taken ill nine and fifteen months previously and had subsequently remained in hospital in England.

No fatal case of the disease is known to have occurred. Observations on morbid changes produced in the tissues by the virus are therefore not available.

The experiments of the War Office Committee and of the American Medical Research Committee show that when conveyed by intravenous injection of infected blood or plasma, or by inoculation of the fæces of infected lice on to the scarified skin, the period of incubation is as a rule from five to nine days, but when transmitted by the living louse the incubation period is from fourteen to over thirty days when estimated from the time the lice are placed upon the subject.

Symptoms.

Prodromal symptoms are rare, and are confined to slight headache or malaise. The onset is usually rapid or even sudden, but in a few cases more gradual. There is shivering or chilliness, and the temperature rises rapidly. At the same time there is in all cases severe headache, and in many sudden weakness or dizziness. Vomiting occurs in about a third of the cases on the first day; anorexia is universal.

A common history is that the patient was awaked in the night by violent headache, and in the morning was unfit for duty, or that at some time in the day he was seized with pain in the head and fell down as if in a faint.

On admission the patient is prostrated, looks ill and is lethargic. He complains of pain in the forehead and in the back, movement of the eyes is painful and there is slight nystagmus on looking outwards. Within a day or two the characteristic rash usually appears, the spleen is felt below the ribs, and there are pains in the limbs. The tongue is coated on the dorsum with a brown or yellow fur, but clean on the tip and edges. The throat is sometimes congested and a dry cough then occurs.

The rash consists of small rosy spots, which are usually round, but sometimes of irregular outline, are effaced by pressure, and are level with the surface of the skin. They come out, like the spots of enteric, in successive crops, and, like them, occur chiefly on the chest and abdomen. They have once or twice been found on the back. But they differ from enteric spots in that they are rather redder than the typical pink enteric spot, have a more indefinite margin, and do not project. They last from twelve to thirty hours, whereas the enteric spot lasts two or three days. Their number may vary from a single spot to many hundreds.

The rash occurs as a rule with fever, and, when the case is of a regular type and relapses can be distinguished, the spots usually appear a few hours before the fever. In a small minority of instances spots are seen on afebrile days.

The rash has been seen on the first day, and as late as the thirty-fourth.

The pains vary greatly in situation, duration, character and intensity. There is no pain that can be considered distinctive. Their persistence, sometimes for weeks, is, however, peculiar to trench fever. The commonest sites of pain at the onset are the head, back and legs. The most constant of all pains is frontal headache. This is practically invariable at the onset, and is often very persistent. Headache is felt in the morning, sometimes for weeks after other pains have disappeared. Pain in the head is sometimes substituted for the word headache by the patient, and probably represents a different kind of pain. It is sometimes felt in other parts of the head than the forehead.

Occasionally pain and stiffness in the nape of the neck occur at the onset simulating cerebro-spinal fever. In a few cases this pain has been so severe that the diagnosis was uncertain until lumbar puncture was performed.

Pain in the chest is not infrequent. It is sometimes felt on one side alone, either in the upper or the lower half. In the latter case the left hypochondrium is a far more frequent site than the right, and the pain is connected with enlargement of the spleen. Occasionally it is felt round the lower ribs on both sides.

Some cases have complained of pain in the right iliac fossa very suggestive of appendicitis. The distinction is usually not difficult to recognize. The iliac pain in trench fever is felt when the skin is even lightly touched, and is not increased by deeper pressure. There is not the rigidity characteristic of appendicitis, and there is no tumour to be felt.

Pain in the back, of an aching kind, sometimes referred to the flanks rather than the loins, is the most common of all pains except headache. It lasts almost as long as headache, coming and going for many weeks.

The lower limbs are far more commonly painful than the upper. In order of frequency the shins and thighs are the most often attacked, next the knees and calf-muscles, and then the hips and ankles. Now and again the instep or the sole of the foot is the seat of pain. Shin pains are about as frequent as backache and occur in about two-thirds of the cases.

The arms are much less frequent sites of pain. Almost every part of them has, however, been attacked—shoulders, upper arms, elbows, forearms, and wrists—in the series of cases observed.

The pains are referred to different structures. The shin pains are referred to the bones themselves, sometimes to definite parts such as the central part of the bone, or the posterior surface.

Pains in the calves, in the thighs, and in the upper arms are referred to the muscles in those situations, and sometimes to particular muscles such as the deltoid or biceps. Pains round the knees are referred to places outside the joint. They are not felt to be within the joint itself. Muscles to which pain is referred, such as the calves or the thigh muscles, are usually tender when squeezed, and there is tenderness round the outside of the knee-joint, especially, it has seemed, at the site of tendinous attachments.

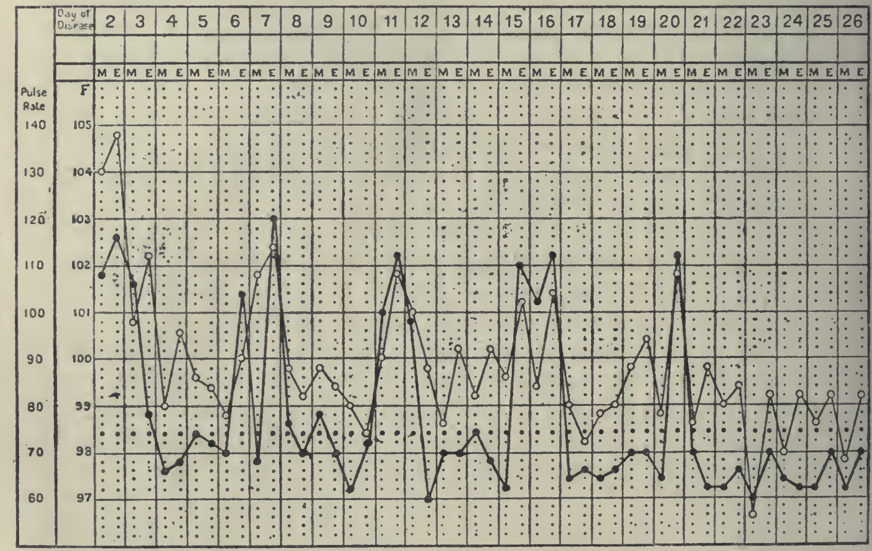

CHART I.—Patient aged 19. Regular form of pulse-rate (light line) rising and falling with temperature (heavy line).

These pains interchange. They will be felt one day in the shin bones, another day in the calves, and a third day in the back. There is no division to be made between cases with bone pains and cases with muscle pains. Nor is there any variety of the disease that can be called shin fever.

There is occasionally superficial tenderness of the skin, in ill-defined areas, and occasionally the site of tenderness is in areas of the trunk corresponding to the zone supplied by one or perhaps two of the dorsal or lumbar nerves.

The character of the pain varies. It is sometimes aching, sometimes boring, and sometimes shooting, in the same patient. The boring pain is commonly in the shins, but these may also ache. Shooting pains are generally felt in the length of the limb.

The intensity of the pain varies also. Many patients are kept awake by it, as it is commonly worse at night. A very few patients have no severe pain. Pains usually disappear in a fortnight, but in some cases last much longer.

The fever reaches its highest point, 102° or 103° F. on the first, or sometimes on the second day, but from this its course is extremely variable. In some cases it follows the typically relapsing form which first drew attention to the disease.

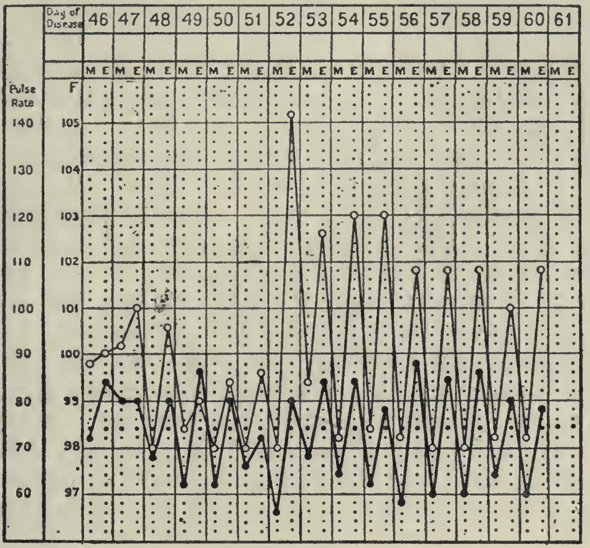

Chart II.

In such cases the peaks of the chart occur usually at intervals of five, or less commonly four, six, even up to eight days. There is a tendency for the highest point to become lower and for the interval to increase as the disease progresses. As many as seven relapses have been seen.

In other cases the relapsing character is less distinct, and in some the fever is quite irregular and may last thus almost six weeks, or after beginning by one or two relapses may later become irregular and continuous.

Even when the temperature is not above 99° F. it is common for the daily variation to be much greater than the normal. There is often a difference of two degrees between the morning and evening level for many days together, as in Chart II.

The American experiments showed that these types do not breed true, that any type may in the next generation produce any other, and that trench fever includes them all.

In the early stage the pulse commonly varies with the temperature, as shown in Chart I, rising to over 100 at the acme and falling to normal in the interval. Sometimes a rise in the pulse-rate may be the only evidence on the chart of a relapse. At a later stage, while in a few cases rates below 60 are seen, it is more common for the pulse to become rapid. Sometimes tachycardia develops gradually, in other cases, as in Chart II, suddenly with palpitation and even dyspnœa. This is more common if patients get up early, but occurs also while they are in bed. It was not seen in the American volunteers who were carefully selected and had not undergone arduous duty.

With tachycardia the heart's apex beat sometimes shifts outwards even to an inch outside the nipple line, and a systolic bruit may be heard for a few days. Præcordial pain has been noticed, but there is no evidence that endocarditis ever develops. The systolic blood-pressure shows a slight tendency to rise as the disease progresses.

Some have reported that the febrile stages are marked by polymorphonuclear leucocytosis, and the afebrile periods by an increase of the mononuclears. But Perkins and Urwick, who made daily counts in many acute cases, showed that polymorphs, mononuclears and lymphocytes all tended to increase in the febrile periods, while the period of convalescence was marked by a gradual rise in lymphocytes. A rise in polymorphs has been found to occur during the few days preceding the onset.

The symptoms connected with the eyes are pain, made worse on movement, and referred to the back of the eyeball, conjunctivitis or "pink eye," and nystagmus on looking outwards, which is probably due to muscular weakness.

The spleen is usually—in 85 per cent. of the experimental cases—palpable at some period of the disease. In about a third of the cases it is felt on the first day, but in some not until much later. The condition may persist for as long as five weeks, but usually disappears in a fortnight. It may reappear again, showing that the organ probably remains enlarged in the interval though not enough to be palpable.

There is no special affection of the gastro-intestinal system. The appetite returns after the first few days. Occasionally the original symptoms recur in the relapse. A slight temporary albuminuria is sometimes found as in other fevers, but no cases of true nephritis were noticed.

In some patients in the early stage a few râles may be heard. Otherwise the lungs are not affected.

It has become evident that in a large proportion of the cases of trench fever invalided home there is a tendency to advance through a subacute towards a chronic condition, with symptoms of disordered action of the heart, and also in some cases neurasthenia.

The symptoms met with may be summarised as follows, in the order of their importance :—(1) Exhaustion ; (2) giddiness and fainting ; (3) headache ; (4) breathlessness on exertion ; (5) pain ; (6) irritability ; (7) lassitude ; (8) sweating ; (9) coldness of the extremities ; (10) palpitation and cardiac irregularity ; (11) fever.

Physical activity is not a necessary factor in the causation of disordered action of the heart, as many cases develop the condition while lying in bed. Tachycardia, however, is usually of vasomotor type, the " sleeping pulse rate " approaching normal, as pointed out by Marris.

In the later subacute stage or transitional stage of the disease the patient presents a well-defined clinical picture. Throbbing headache is complained of, the face is flushed, the pupils dilated, the skin warm, profuse sweating occurs on slight exertion, marked tremor is present. Sometimes constant nausea is felt and fainting frequently occurs. When the chronic stage, or stage of disordered action of the heart has been established this extreme instability of the nervous system is less well marked. The patient no longer tends to swing from states of excitement to states of collapse. Another and different clinical picture is met with, corresponding to the entity which has acquired the title of " neurasthenia," qualified by some with the words " of vasomotor type." No matter what name may be given to it, it will be found that there occur brisk reflexes, coldness and blueness of the extremities, irritability of temper, inability to fix attention for long periods, and exhaustion after sustained effort far in excess of that evoked by the same effort in healthy men.

Breathlessness on exertion, palpitation, præcordial pain and giddiness are features of both subacute and chronic conditions.

The temperature in these chronic cases varies considerably ; definite fever waves lasting from a few hours to several days occur at irregular intervals, which frequently are to be measured in months. Most cases show an increased daily range of temperature, and this is probably the most characteristic condition, the morning reading being definitely subnormal, the evening rise barely reaching fever height, but the daily swing frequently exceeding two degrees Fahrenheit.

Invaliding.

It is important, but at the same time it is difficult, to give an accurate estimate of the period for which trench fever incapacitates. When the disease first appeared it was customary to look upon it as a slight affair, but it was soon evident that in some cases it was much more serious.

The best unselected groups of cases from which such an estimate can be formed are those cases which were under special observation by the committee in No. 12 Stationary Hospital at St. Pol; the experimental cases of the American Research Committee; and a series of 822 cases specially observed for this purpose in 1918 at Boulogne.

The St. Pol cases numbered 348. All were admitted in the acute stage, many on the first day. When possible such cases were retained for several weeks. At times pressure on beds compelled evacuation.

181 = 52 per cent. were discharged to duty; 96 within six weeks, and 85 later than six weeks owing in 44 cases to disordered action of the heart, in 14 to continuance of fever or pain.

167 = 48 per cent. were evacuated to England; 73 owing to want of room, and 94 later than the fifth week for symptoms, namely, 66 for disordered action of the heart, 25 for continuance of fever or pain.

The Americans give no statement of the length of their cases but, having had some cases of relapse after long intervals, conclude " that long periods of latency may exist, and that with our present methods of observation we have no certain means of telling when the patient has completely recovered." Their cases were, as above mentioned, remarkable for the absence of disordered action of the heart.

At Boulogne, out of 822 cases which were carefully observed for the special purposes of determining the resulting incapacity and invalidism—

684 = 83·2 per cent. were discharged to duty in an average of 60 days.

92 = 11·5 per cent. were evacuated to England, including 21 for disordered action of the heart, 37 for continuance of fever and 28 for debility.

46 = 5·2 per cent were sent to a medical board to be reduced in category partly, at any rate, for other causes than trench fever.

Of the 92 cases sent home 70 per cent. were traced one year later. This was done partly by scrutiny of hospital case sheets, but chiefly and in every case by a return filled in by the patient himself, who would naturally emphasize any persistent disability.

It was found that 12 per cent. were quite fit. The rest all complained of weakness, loss of weight, and of various pains. The symptoms of disordered action of the heart were not prominent in the replies made by the men. Out of the total, 56 per cent. had not been regarded as eligible for any pension. The detailed figures were :—

Recurrent fever ..	None in 42 per cent. ; slight in 36 per cent. ; more severe in 11 per cent. ; not ascertained in 11 per cent.
Pensions granted ..	None in 56 per cent. ; for disordered action of the heart in 19 per cent. ; for debility in 13 per cent. ; for myalgia in 6 per cent. ; cause not stated in 6 per cent.

The grade of discharge from the army was found to be of no comparative value owing to the various classifications employed. Serious disability, requiring evacuation to England, therefore, had developed in 11·5 per cent. of the total of 822 cases, and 5 per cent. were still pensionable invalids after the expiration of one year.

Similar cases reached the special trench fever wards at Hampstead, and a careful analysis of their after-histories was made by Byam and his co-workers.

Over 1,100 trench fever cases were studied, and their disposal on discharge from hospital was as follows :—

To duty	5·9 per cent.
To lower category	5·0 ,, ,,
To command depôt	9·3 ,, ,,
To convalescent hospital	72·4 ,, ,,
To civil life as permanently unfit for military duty	7·2 ,, ,,

The average duration of disability on day of discharge from Hampstead hospital was 4·5 months.

Of the above cases 402 were reported on with regard to disordered action of the heart, with the following results :—

D.A.H. due to all causes	155=38·5 per cent.
D.A.H. due to causes other than trench fever	44=10·9 ,, ,,
D.A.H. due to trench fever with onset of D.A.H. before admission to Hampstead	69=17·1 ,, ,,
D.A.H. due to trench fever with onset of D.A.H. after admission to Hampstead.	42=10·4 ,, ,,
Average day of disease on which D.A.H. was first recorded in cases developing D.A.H. in Hampstead Hospital	27·3
Extremes of onset of D.A.H.	15th–62nd day.

Febrile relapses were found to occur in all types of cases invalided to England, 8 per cent. showing a definite febrile relapse with temperature of 102° F., or more after an afebrile period varying from two to five months, during which time the temperature had not exceeded 99·4° F.

The statement has been made that all but a very small percentage of trench fever patients made a good, complete and rapid recovery. While this is true of about 85 per cent. in the acute disease, as has been stated above, it does not in any sense apply to the chronic disease, as is abundantly proved by these figures, and Byam states that " the average of definitely known disability, lasting for over six months, cannot be reduced to anything less than 37 per cent. of the chronic cases, or considerably more than 5 per cent. of all the infected." In the year 1920 there were about 6,000 pensioners who attributed their disability to trench fever, and a very small proportion, less than 5 per cent., of the cases of disordered action of the heart were attributed to the same cause.

The following table is based on a series of 2,000 cases of trench fever treated in military hospitals in France and Salonika over the period 1915–1918, and shows the number of days patients suffering from trench fever were retained under treatment in those theatres of war. The information has been compiled by the Medical Research Council from index cards and admission and discharge books.

No. of Days under Treatment in a Series of Cases of Trench Fever.

Force from which derived.	Number of Cases.	Total average of Days under treatment.	Average Number of Days under treatment.
France	1,944	155,463	80
Salonika	56	1,169	20·9

Prognosis.

With regard to prognosis, trench fever is practically a non-fatal disease, but may result in prolonged ill-health in from 10 to 20 per cent. of all those affected.

During the war some cases were observed where evidence of a persistent infection lasted for three or four years, and in the present state of knowledge it is impossible to tell the ultimate fate of such sufferers. Certain it is, however, that field service conditions were not alone responsible for the prolonged disability, as similar symptoms were occasionally observed to follow experimental infections in the best hygienic surroundings.

Age, in its reaction to the demands of modern warfare, produces a man so diminished in recuperative capacity that when infected he is less able to throw off the disease than the younger man. Men of thirty-five years and over, when infected in the field, usually required six months or more to complete recovery.

A bad past medical history is of the greatest significance. The analysis of a group of 236 chronic cases showed that 18·2 per cent. were physically unfit when they contracted the disease. The man who gives a history of former attacks of trench fever is particularly prone to pass into the chronic stage.

The earlier the patient gets to bed after the onset of the attack, the more likely is he to make an early and complete recovery. In the chronic stage a steady gain in weight constitutes the most reliable guide to a favourable prognosis. A constantly declining weight curve is an unfavourable indication.

Diagnosis.

With regard to diagnosis, as has been noted above, acute pain is felt by some patients in the right iliac region. This has led occasionally to a diagnosis of appendicitis and even to operation. The points of distinction have been mentioned already.

Attention has also been drawn to the fact that cases of trench fever occasionally have pain and stiffness in the neck so severe as to simulate cerebro-spinal fever, and that the distinction must be made by lumbar puncture.

The diagnosis from influenza is much more difficult. At the onset the two may be practically indistinguishable,* but the characteristic rash, the relapsing form, and in a typical case the rather peculiar pains of trench fever will generally render the diagnosis easy within a week. Before influenza became epidemic the diagnosis of trench fever was frequent and unhesitating. After influenza appeared trench fever was a rare cause of admission and every indistinct fever with pain was called influenza. It can hardly be doubted that the two often were, and often will be, confused.

Treatment.

With regard to treatment, no remedy has been found that will cure the disease. Quinine, arsenic, salvarsan, perchloride of mercury, antimony and colloidal silver were tried in France and in England, but without satisfactory results. As is usual in such cases good effects were reported but were not corroborated. Opium in the form of Dover's powder or morphia may be used in case of severe pain, especially if sleep is disturbed.

Experience shows that, in order to return men to duty as soon as possible, the surest course is to treat the disease seriously, to admit the patient to hospital at the earliest possible date, to keep him in bed for twenty-one days at least, and for a week after he has shown any symptoms, and to watch carefully the effect of getting up upon the circulation. The Boulogne observers conclude as follows :—

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* See Influenza, p. 205.

" The best general means are probably much the same as those which were used with such admirable results in France in 1918 for the treatment of relapsing malaria cases from the Mediterranean—namely, to take the patient away from hospital environment and slowly to restore his general resistance by food, fresh air, and light exercise until the infection is overcome. Few cases required prolonged rest in hospital, and the majority can be returned soon and successfully to full duty. Such a view of their normal disposal is obviously governed only by a consideration of the invalidism of the casualties who have already gone sick. It is not concerned with the other aspect of the question, as to whether an early return of such casualties to the lice-infested areas at the front may not be a disadvantage because it may re-introduce possible sources of infection to other healthy troops."

The preventive treatment consists in freeing the men as far as possible from lice.

It is remarkable that there has been no spread of the fever in the United Kingdom since demobilization. The louse does not transmit the poison to its offspring, and the degree of lousiness of the civil population is not to be compared with that of the army. The close contact of a patient infested with lice, which is a necessary condition of infection, is therefore seldom present in the United Kingdom.

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McNee, Renshaw & Brunt	Trench Fever	Jl. of R.A.M.C. 1916, Vol. xxvi, p. 490. B.M.J. 1916. Vol. i, p. 225.
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CHAPTER XVII.

JAUNDICE.

JAUNDICE is not a disease in itself; it is a symptom that may appear in many different diseases, but it proves that such disease has directly or indirectly affected that particular function of the liver which deals with the excretion of bile-pigment.

Jaundice was seen under many conditions of disease during the war. Some of these, such as that associated with poisoning during the manufacture of trinitrotoluene, or in the use of a particular varnish containing tetrachlorethane for aeroplane wings, were relatively new to medical experience. Spirochætal jaundice had been seen before under the name of Weil's disease; but its pathological cause was only discovered early in the war by workers in Japan, and their conclusions revealed what therefore became practically a new infectious malady, though fortunately it never produced any serious amount of inefficiency.

Apart from the cases of poisoning by T.N.T. amongst civilians, which was soon eradicated when its nature had been determined, the most serious loss of man power to the army by invaliding on account of diseases associated with jaundice was due to the extensive epidemics of campaign jaundice seen in Gallipoli, Egypt and Mesopotamia. The exact nature of this epidemic infection was never ascertained, though it appeared to follow upon intestinal and blood infection by some organisms of the coli-dysentery group. Similar outbreaks had occurred in previous wars, for example, during the South African War and in the American War of 1862, when certain camp areas showed a particularly heavy incidence.

The general trend of pathological work in the last few years has been to emphasize the view that jaundice in most diseases is the result of direct damage to the liver. In the gravest examples of such disease the liver cells are found to be necrotic, and the liver may be in the condition spoken of as acute yellow atrophy. Even in these cases, however, there are irregularly scattered areas of less severe cell destruction, where bile pigment continues to be formed, but cannot escape down the bile capillaries and so finds its way into the blood stream. To use the term "obstructive jaundice" for such forms, where no distension of the larger bile ducts can be discovered, is to stretch a classification unduly. It is better to confine the term to those forms of disease in which the liver cells are at first normal and the jaundice arises simply because the efflux of bile is directly blocked somewhere in the main ducts.

An intermediate group of diseases has been repeatedly described in which the destruction of liver cells is less manifest, but inflammation of the finer bile ducts leads to their blockage by inspissated bile. These are generally spoken of under the heading of "obstructive cholangitis," and the tendency has been to classify them with the true forms of obstructive jaundice. It is better, however, to assimilate them to the group of toxic hepatitis, realizing that the injuries causing inflammation of the bile ducts may often pass deeper into the parenchyma of the organ and damage the liver cells, just as in the lungs bronchitis may readily pass into broncho-pneumonia.

The value of recognizing that jaundice is in most diseases caused by hepatitis, whether this be from poisons or from an immediate infection by organisms, is that it enables one to rise to a wider view of each intoxication or infection as probably affecting other organs, for example, the kidney with albuminuria and the spleen with enlargement. Thus in spirochætal jaundice the liver is infected and jaundice appears, while the hepatic cells may show all conditions ranging from no microscopic change up to extreme necrosis and dissociation. But it is easy to conceive how a blood infection by these spirochætes may cause inflammatory disease of other organs without the appearance of jaundice, and such forms of this spirochætosis did as a matter of fact occur. It is interesting to note the frequency with which spirochætal blood infections may be associated with jaundice from hepatitis, as in spirochætosis ictero-hæmorrhagica, in relapsing fever, in yellow fever, and often in syphilis.

The various maladies in which jaundice was seen to occur during the war are recapitulated in the following list, with brief remarks, except for certain groups that are dealt with separately in detail.

A. Jaundice due to excessive destruction of red blood corpuscles and consequent overloading of the liver with derivatives of hæmoglobin. The stools usually show a full dark or yellowish colour. This form of jaundice is found in :—

(1) Blackwater fever, and in ordinary malaria, where it was seen occasionally but was not of ominous prognosis.

(2) Poisoning by arsine (AsH_3) fumes. The arsenic substances employed in gas warfare did not cause hæmolysis and jaundice ; but some cases of arsine poisoning were met with in the navy, where the gas had been generated from the use of impure chemicals for accumulator batteries in submarines.

(3) Some gas gangrene and some streptococcal infections causing rapid anæmia, and, with this, light jaundice was occasionally observed as an index of the grave nature of the infection. It is doubtful whether such jaundice should be ascribed to the hæmolysis or to a direct damage of the liver.

B. Obstructive jaundice caused by blockage of the main bile ducts while the liver cells are at first normal and healthy. The stools are finally a chalky white.

Occasional examples due to gall-stones or tumours were of course seen, but none of the ordinary diseases with jaundice that occurred during the war could be fairly placed in this group.

C. Jaundice associated with hepatitis, this being either a direct inflammation or necrosis of liver cells, or a cholangitis with obstruction of the finer bile ducts. The stools may range from normal to a greyish-white colour. The two forms are frequently mingled, so that it is hard to draw a line between them except in the histological examination of any individual case. Even when an infection reached the liver by ascending the bile passages from the intestine it none the less caused some hepatitis as well as cholangitis, and the hepatitis and similar inflammatory changes in other organs of the body were the really serious factors in the disease, while the jaundice was only a colour smeared over the essential details of the clinical picture. Portal obstruction and ascites were seen to develop in a few of the chronic cases of some of these maladies, but there has been no satisfactory evidence that any of them were particularly liable to be followed by a slowly progressive hepatic cirrhosis.

Jaundice of this nature may be classified as follows :—

1. Spirochætosis ictero-hæmorrhagica (Weil's Disease). The closely allied disease, yellow fever, did not appear among the British troops.

2. Epidemic catarrhal jaundice. C. J. Martin has argued with great weight of evidence that this infection should be regarded as one of a generalized character, like that in spirochætal jaundice, with the possibility of hepatitis, albuminuria, and splenic enlargement occurring in it.

3. Simple catarrhal jaundice. These sporadic cases of mild jaundice were frequent in military just as in civil experience. They appeared to be infective, and sometimes lightly contagious. Their relationship to epidemic jaundice is uncertain.

4. In typhoid and paratyphoid fevers. Jaundice was rare in dysentery.

5. In influenza and lobar pneumonia. Jaundice was not often seen in France as a concomitant or sequela of influenza

until January 1919. It was, however, reported in the transport "Nestor," bringing troops from America, as early as September 1918. During the wave of influenza that began in January 1919 it became much more common. It occurred at any stage of the fever, sometimes in the first few days, sometimes not until convalescence was advanced. In the latter case it has been ascribed to the increase in diet, but there seems to be no good ground for this suggestion, and probably, like that which occurred earlier in the disease, it was due to the influenza virus or organisms associated with that infection. It had the appearance of an ordinary catarrhal jaundice, was not attended with any severe symptoms, and did not in any way affect the prognosis.

Such cases were few compared to the number of cases of influenza, and there was seldom an opportunity of making an examination of the organs. In one case which died deeply jaundiced in the first week of the fever, with severe pulmonary lesions, the bile passages outside the liver and the duodenum itself showed no abnormal appearances.

The occasional occurrence of jaundice in lobar pneumonia had been observed before the war and was seen during it, perhaps more frequently in pneumonia of the right lung.

6. In relapsing fever. This complication of a blood infection by Obermeier's spirochæte was not uncommon. Captain Nicholson observed jaundice in 64 per cent. of two hundred and forty-one cases in hospital at Baghdad, but the incidence was usually much lower than this. White as well as coloured troops were affected. The jaundice occurred early and was sometimes deep, but it did not affect the prognosis, for there was neither anæmia with it nor severe degeneration of the hepatic cells.

7. In salvarsan poisoning. Syphilis itself, in either the secondary or tertiary stages, may be associated with moderate jaundice. But examples were seen of very severe or fatal jaundice, with intense destruction of the liver, which were directly caused by salvarsan treatment. The symptoms might appear at the end of a course of treatment, or even some weeks subsequently.

8. In trinitrotoluene poisoning. From the handling of this high explosive the substance is absorbed through the skin, and in susceptible persons may cause extreme destruction of the liver. In the twelve months of August 1916 to 1917 there were 238 cases of this toxic jaundice among munition workers in England, with 75 deaths.

9. Poisoning by tetrachlorethane from the use of aeroplane varnish. In this case the poison was absorbed through the

lungs. The histological injuries, with associated degeneration in the heart and kidney, were similar to those with T.N.T., and in chronic cases there was considerable cirrhosis of liver.

Delayed chloroform poisoning was sometimes observed to cause a similar toxic jaundice.

10. Intestinal worms, such as ascaris, were occasionally the cause of a secondary jaundice.

Of these the spirochætal type, the epidemic catarrhal of campaigns and the jaundice associated with the enteric group of fevers were distinct forms of jaundice which occurred during the war, and call for detailed description.

SPIROCHÆTOSIS ICTERO-HÆMORRHAGICA.

Spirochætal jaundice or spirochætosis ictero-hæmorrhagica is caused by a micro-organism identified in November 1914 by two Japanese workers, Inada and Ido, and named by them *Spirochæta ictero-hæmorrhagiæ.* They showed the presence of this spirochæte in the liver of a guinea-pig which had been inoculated with the blood of patients suffering from a form of infectious jaundice, and they also obtained the organism from the blood and urine of the patients themselves. By the courtesy of Dr. Flexner of the Rockefeller Institute, an early account of their results was forwarded to the Medical Research Committee and reached France in February 1916. In the summer and autumn of 1915 the attention of medical officers in France had been arrested by the occurrence of severe cases of jaundice in which there were high fever, hæmorrhages, enlargement of the liver, and a tendency to febrile relapses, the features of which conformed neither clinically nor bacteriologically to those of typhoid fever. In the autumn of 1915 cases of this kind were collected for purposes of closer study, and in April and May 1916, when the Japanese investigation became known, the *Spirochæta ictero-hæmorrhagiæ* was shown to be the cause of the disease in these military patients.

The disease occurred in the French and German as well as in the British armies on the Western front. It seems probable from Martin's account that it also occurred in Gallipoli, though he had not there facilities for animal experiments.

Ætiology.

Japanese workers were the first to point out that this spirochæte is found in the kidneys and urine of rats. They were able to show the presence of *S. ictero-hæmorrhagiæ* in 38 per cent. of the field rats coming from areas in which jaundice was epidemic, and they suggested that the infection might be conveyed by the rat's urine, directly or indirectly. Noguchi has shown that American wild rats contain this organism in their kidneys; Coles found it in nine out of a hundred rats investigated in England; and Stokes showed that six out of fifteen rats caught in the areas in Flanders, in which jaundice was endemic, contained in their kidneys a spirochæte capable of producing the disease in the guinea-pig. Rats act, then, as reservoirs for the infective agent.

It is easy to see how the infective urine of rats can convey the disease by fouling the water and food in the trenches. Nearly all the cases on the Western front occurred in men who were, or had lately been in the trenches; and the disease was shown to be more prevalent in wet than in dry trenches.

The rats do not appear themselves to suffer from the presence of the spirochæte. At the Wellcome Bureau of Scientific Research, no obvious changes were found in the kidneys or in other organs of infected rats.

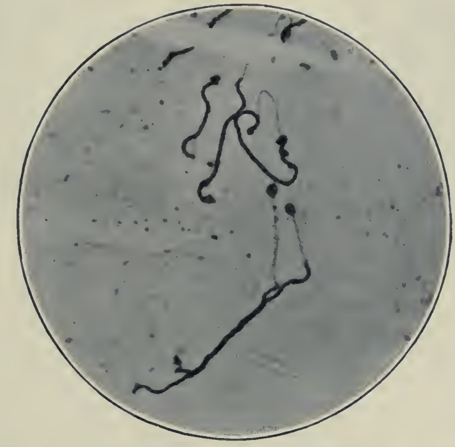

FIG. 1.—*Spirochæta ictero-hæmorrhagiæ.* (Pettit.)

As the result of later investigations on the parasite of icterohæmorrhagic jaundice, Noguchi found no differential features between the Japanese, European and American strains. He has shown that, both morphologically and in its resistance to destruction by a 10 per cent. solution of saponin, it is unlike all previously described spirochætes. For this reason he prefers to place it in a separate genus under the name *Leptospira icterohæmorrhagiæ.*

The infecting spirochæte varies in length from 4μ to 25μ, the average being 8μ to 9μ; its thickness is estimated by the Japanese workers at $0{\cdot}25\mu$. The ends are sharp, pointed and often hooked. Terminal flagella of varying length and ending in circular knobs have been described, but their significance is unknown.

This organism shows irregular undulations, usually composed of two or three large, or four or five smaller, waves.

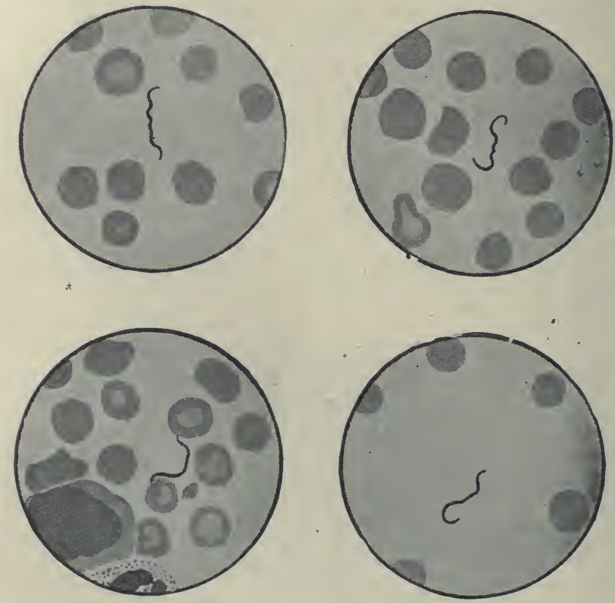

FIG. 2.—*Spirochæta ictero-hæmorrhagiæ* in blood of guinea-pig experimentally injected. (Bedson.)

Now and then forms are seen in which the waves are more numerous and regular, like those of *Treponema pallidum*. Other variations in shape are sometimes seen ; round or oblong granules, three or four in number, may appear within some of the spirochætes. The organism may be grown in various media, liquid and solid—blood agar and gelatine, human serum, diluted ox serum and ascitic fluid. The optimum temperature is about 27° C., but growth occurs at temperatures between 22° C. and 32° C. The growth is at its height about the tenth day in primary culture, and from the fourth to the sixth day in subsequent subcultures ; by the end of three weeks the culture is usually dead. The presence of contamination hinders or destroys growth. This spirochæte has, in general, strong vitality ; it will remain active in tap water exposed to wintry weather for many days ; yet sometimes it will suddenly die out under good conditions for no apparent reason.

The antiserum for spirochætal jaundice, first prepared by Martin and Pettit, contains a specific agglutinin in addition to spirochæticidal immune bodies. The serum of convalescents possesses also the power of clumping the spirochætes; this agglutination thus provides an additional diagnostic test. The agglutinating power of the serum of convalescents may rise to a titre of 1 in 500 or 600, whilst normal serum and the serum of syphilitic patients are without effect on S. *ictero-hæmorrhagiæ.*

Attempts to reproduce the disease in animals have shown that the guinea-pig is extremely susceptible, but the mouse, rat, rabbit and monkey are also prone to the disease. The guinea-pig can be infected by intraperitoneal injection of the patient's blood or urine, but where blood is used it must be taken early in the disease. The disease in the guinea-pig incubates for from six to thirteen days, a week being a usual period; it is characterized by jaundice, hæmorrhages (those in the lungs being especially characteristic), conjunctival congestion, albuminuria and pyrexia. It is nearly always fatal. Jaundice appears when the temperature has reached its maximum (103° to 106° F.), and the animal then becomes more acutely ill. Twenty-four hours later there is a fall of temperature to subnormal, followed usually by collapse and death. Spirochætes appear in the blood with the onset of fever, and in the urine soon afterwards; they are plentiful, too, in the liver, kidneys, and suprarenals.

Symptoms.

The following clinical description of spirochætal jaundice is drawn in the main from the study of cases occurring among soldiers in France and Flanders. The patients were almost invariably attacked by the disease either in the trenches or immediately after having left them.

The period of incubation is not constant; its limits have not been determined, though they are probably six to twelve days. In a case of accidental laboratory infection, recorded by Martin and Pettit, the term of incubation was fixed between six and eight days.

The onset is more often sudden than gradual; early symptoms are shivering, headache and body pains, great prostration, vomiting and diarrhœa. The temperature rises quickly to 102° F. or higher. During the next three or four days the conjunctivæ become injected, and herpes (often hæmorrhagic) appears on the lips in some 40 per cent. of the patients. Bleeding, while uncommon in mild, is usual in severe cases; it may come from the nose, lungs, stomach or intestine, or it may take the form of a purpuric rash. Early in the illness slight hæmoptysis is a valuable diagnostic sign. Hæmorrhage generally precedes jaundice in order of appearance.

The jaundice appears, as a rule, on the fourth or fifth day of illness, but it may be as early as the second or as late as the seventh day; it reaches its height about the tenth or twelfth day. Sometimes it is intense and the skin has the greenish hue seen in complete obstruction of the common bile duct. Constipation is pronounced; the stools may be clay coloured, but are more often light brown. Tenderness in the upper abdomen is usual; the tongue is furred, dry and brown, and in severe cases there are sordes on the lips. The liver is frequently enlarged as much as two or three fingers' breadth below the costal margin, but the spleen is seldom palpable. The lymphatic glands in the axillæ and groins are sometimes enlarged and shotty.

In severe cases signs of bronchitis are usual; the respiration rate may rise to 30 or even higher, and when death is impending the range and character of the breathing may be modified as they are in cases of uræmia and diabetic coma. The pulse is slow in proportion to the pyrexia, a rate of 75–85 being quite usual.

The early weakness and prostration are characteristic of this disease. Frontal headache and aching behind the eyeballs cause much distress at first, but diminish as the days pass. Dawson and Hume found vomiting a symptom in 60 per cent. of cases and Ryle in 76 per cent. The muscular pains last longer and are at times intense. The patients complained of feeling as if they had been beaten and the muscles were tender on pressure. Twitchings and convulsions may precede or accompany the coma of fatal cases. The urine contains bile in abundance, which may persist for four or five weeks. Albuminuria is usually present and urinary casts, hyaline, epithelial and granular, are common. French authors lay stress on the evidences of renal insufficiency. Ryle found acetone to be present in 16·3 per cent. of his cases.

The course of the illness varies with the severity of the attack. In an acute case irregular pyrexia persists for ten days to a fortnight, and falls by lysis. Sometimes there is a secondary rise of fever about the beginning of the third week, but without exacerbation of symptoms or increase of jaundice. The temperature may fall about the tenth day, when the jaundice reaches its height; or it may fall earlier, while the jaundice is still deepening. Convalescence is slow, but recovery is usually complete.

Not all cases of this disease conform to the foregoing picture; many are like the following, mild and less defined in their manifestations, and therefore more difficult of detection.

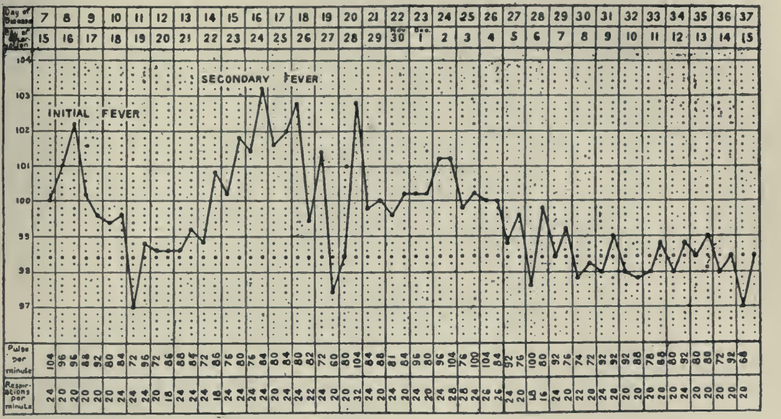

CHART I. CASE 1.

Case 1.—Aged 38. Onset sudden, with vomiting. Day 3: dark urine. Day 4: drowsy; ill; reported sick. Day 7: brown tongue; jaundice + + epigastric tenderness. Liver + two fingers; spleen 0. Urine—albumin, bile, casts. Stools contained some bile. Blood—R.B.C. 5,200,000; W.B.C. 13,000. Days 7 to 18: toxic; jaundice + +. Day 19: gall-bladder drained (operation). Day 22: jaundice less; condition improved. Day 32: convalescent.

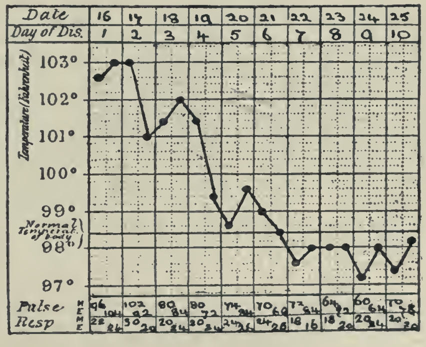

CHART II. CASE 2.

Case 2.*—Sudden onset; pains head and body; vomiting. Day 6: suffusion of conjunctivæ, slight jaundice; liver 0; spleen 0. Day 9: jaundice + + drowsy. Day 10: condition improving, W.B.C. 8,500. Day 12: typical spirochætes found in urine.

Jaundice is a usual though not invariable feature of this disease. Cases 3 and 4 illustrate the variety in which it is absent.

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* Compare with this enteric jaundice, page 401. Chart VIII.

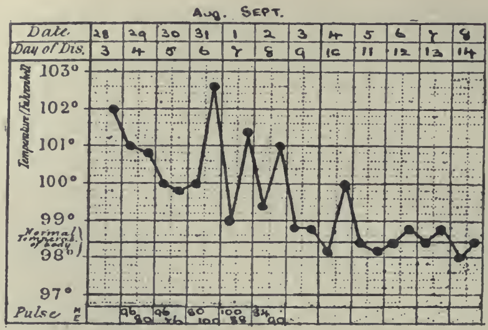


CHART III. CASE 3.

Case 3.—Onset sudden; feverish; generalized pains; lassitude + giddiness. Day 3: cough; herpes labialis. Day 4: spirochætes in blood; pains continue. Day 10: patient improving. Day 14: typical spirochætes in urine.

Case 4.—Sudden onset; headache; body pains; photophobia; vomiting. T. 104·2°; patient very ill. Days 2 to 5: conjunctival suffusion; herpes labialis; vomiting + no hæmorrhages. Day 14: convalescence. Day 20: relapse of fever and pains.

Inoculated guinea-pig developed jaundice. Spirochætes in patient's urine until the end of the ninth week.

In some cases nephritis is a prominent feature.

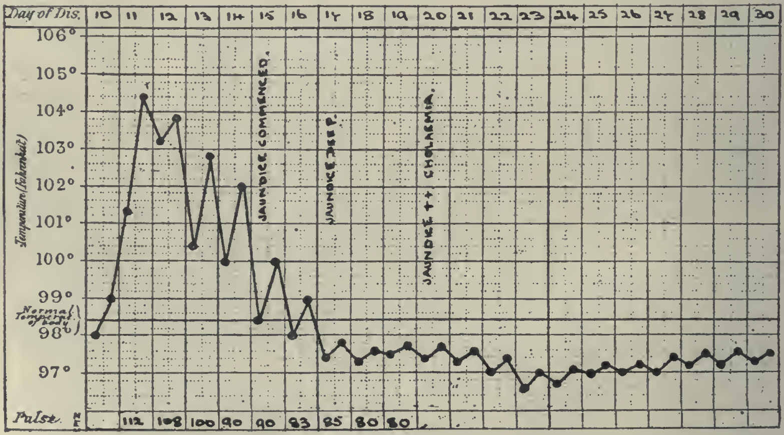


CHART IV. CASE 5.

Case 5.—Onset and early days; body pains; mild headache; transient œdema. Urine—albumin and blood. Day 10: looked ill. Urine—albumin, blood and casts. Day 11: fever. Urine as before. Day 15: jaundice faint. Day 17: jaundice deep. Urine; blood 0; albumin—trace. Days 17 to 30: weak; wasted; drowsy; cholæmic. Picture resembled spirochætosis. Slow recovery. Bacteriological data; enteric negative. Typical spirochætes in urine on three occasions.

In the following cases the result was fatal:—

Case 6.—Onset: vomiting; pains in leg; fever. Day 3: hæmatemesis (½ pint). Day 4: ill; drowsy. Day 7: jaundice rapidly + +. Day 10: jaundice + + +; abdominal distension; slight cough; bloody sputum; liver + 3 fingers; spleen 0. Urine—bile + albumin + no casts. Stools, clay. R.B.C. 3,000,000. W.B.C. 20,000. Day 14: drowsy; weak. Day 20: temperature normal; jaundice less. Days 22 to 29: drowsiness + + picture of diabetic coma; jaundice diminishing; general clonic convulsions on 27th day; death in coma.

Case 7.—Onset acute; pains; repeated vomiting; very ill; vomiting continued until 14th day. Jaundice appeared 5th day. Liver + 2 fingers; spleen 0. Urine—albumin trace; casts + +. Stools almost clay-coloured. Blood—W.B.C. 22,500. Drowsy throughout; died on 14th day from toxæmia.

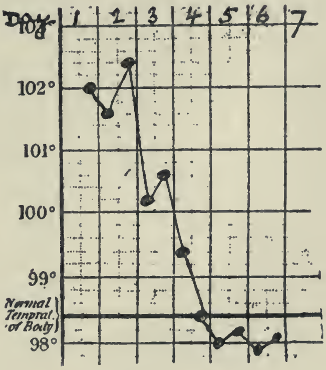


Chart V. Case 8.

Case 8. Onset: head and body pains, weakness, chilliness. Temperature 102°. Days 2 and 3: repeated vomiting. Day 3: herpes labialis; jaundice. Day 4: temperature normal; jaundice markedly increased; liver and spleen not palpable; patient much worse. Day 5: hæmatemesis; albumin + + epithelial and erythrocytic casts, no spirochætes; dry brown tongue; tonic convulsions; general condition grave. Day 6 and onwards: epistaxis, hæmatemesis, melæna, purpura. Guinea-pig inoculated seventh day: negative. Day 12: death from toxæmia and anæmia. Urine contained characteristic spirochætes.

Clinical Pathology.

Apart from the finding of the spirochæte, examination of the peripheral blood reveals certain abnormalities.

In severe cases there is slight anæmia, the average red cell count being 4 to 4½ million per c.mm., and the hæmoglobin is reduced to 80 or 90 per cent. Some cases become very anæmic. There is invariably a leucocytosis, amounting in some cases to 25,000 per c.mm. This may, however, be absent or slight in the early stages, according to Stokes. The differential count shows a relative increase of the polymorphonuclear leucocytes to 75–80 per cent. The fragility of the red corpuscles is either normal or slightly diminished. No abnormal red cells have ever been detected. From this it may be concluded that the jaundice is not of hæmolytic origin.

In man the blood infection is brief and relatively light, and the spirochæte is difficult to find in blood films or cultures. After the fifth day of disease, recovery of the organism is rare, but intraperitoneal inoculation of a guinea-pig may yield a positive result up to the seventh, eighth or ninth day. Later than that the result is always negative.

Reproduction of the disease in the guinea-pig by injection of the patient's blood or urine is beyond doubt the most satisfactory and convincing diagnostic test we at present possess. Since, however, the blood is infective only in the early stages of the disease, while the infectivity of the urine varies much, this method of diagnosis as a practical measure has its limitations.

Leptospira ictero-hæmorrhagiæ, as shown by the Japanese, is eliminated chiefly by way of the kidney. From the ninth day onwards it can be demonstrated microscopically in the urine. At first it appears in small numbers only, the number gradually increasing to a maximum about the thirteenth to the fifteenth day of the disease, to diminish again and finally disappear from the urine in the fifth or early in the sixth week of illness. It does not suffice to examine the urine on one occasion only; several examinations at intervals of two or three days may be necessary before the organism is found.

Spirochætes may be present in the urethral meatus of healthy persons. It is necessary, therefore, to eliminate this source of error by washing the glands and meatus, and then catching the middle portion of the urine in a sterile flask. They are never excreted from the kidney in health. Spirochætes have, however, been found in a few cases of pyrexia of uncertain origin, and in relapsing fever. The final test depends upon the effect of inoculation upon the guinea-pig, which is immune to any except the *Spirochæta ictero-hæmorrhagiæ*, but, if that form is injected, reproduces the characteristic signs of the disease.

Morbid Anatomy.

In two of the above fatal cases the mucous membrane of the duodenum was very œdematous and congested, its colour resembling a dark-blue plum. The ampulla of Vater was swollen and congested, and around it there was a raised area of red and injected mucous membrane. A lesser degree of congestion and œdema was seen in the first three feet of the jejunum and in the stomach, but the rest of the intestines were unaffected. Enlarged lymph glands were seen at the edge of the lesser omentum and about the bile ducts. The last portions of the common bile and pancreatic ducts, when laid open, were of normal appearance except the termination in the ampulla of Vater, which was swollen, congested and blue. That no inflammation of the duodenum occurs in this disease is borne out by the results of duodenal intubation; the withdrawn duodenal contents have been shown to contain polymorphonuclear leucocytes and large mononuclear cells—clearly the products of local inflammation. It would seem to be clear, therefore, that in some instances the spirochætal infection localizes in the duodenum; whereas in others the duodenum is normal in appearance and the chief changes are found in the liver and less often in the kidneys.

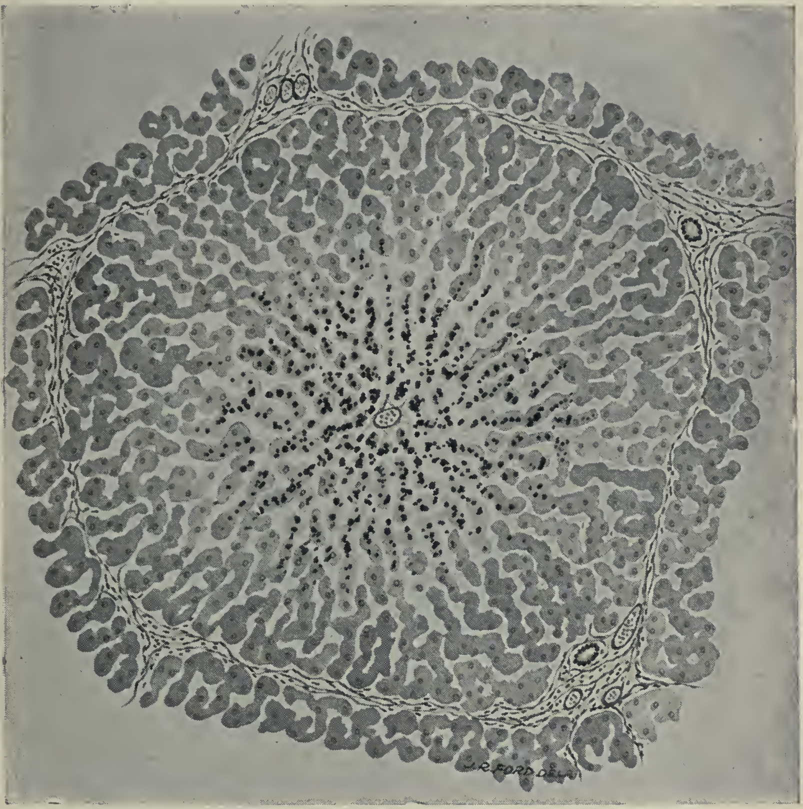


FIG. 3A. Section of liver from a case of spircchætal jaundice.

Of five post-mortems studied by Dawson and Hume, two had a duodenal change, while the bile ducts, the pancreatic duct and livers showed no change ; one had duodenal change and slight liver changes ; one showed no morbid appearances in either duodenum or liver ; one showed no duodenal changes but marked disorganization of the liver.

The changes in the liver are not uniform. To the naked eye they are often slight or insignificant, the pattern and texture appearing normal, though some discoloration due to bile stasis is not uncommon. On microscopical examination the appearances vary (Figs. 3A, 3B). The cells of the lobule may be natural in size, shape and arrangement, and apart from evidence of biliary stasis the only abnormality may be the presence of collections of cells in the portal areas, such as occurs in many other diseases.

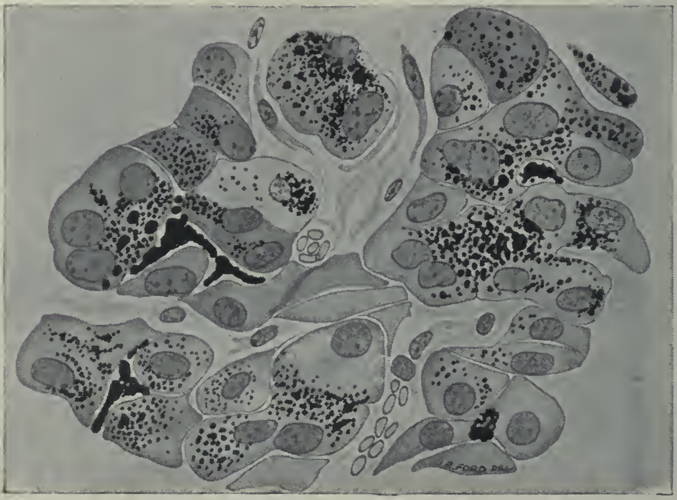


FIG. 3B. Part of same section more highly magnified. The liver cells and their arrangement appear normal. Biliary stasis is evident.

In other cases definite changes are found on microscopic section. There is some loss of lobular pattern, the cells show undue variation in size and shape, and here and there the nuclei are large or multiple, and a few mitotic figures and vacuolation of the cytoplasm can be observed (Fig. 4). Or, again, these changes just described may be more advanced, dissociation of cells may be pronounced, and the cells in the centre of the lobules show granular degeneration (Fig. 5). These changes suggest the effect of damage not great enough to cause extensive necrosis, but sufficient to stimulate cell growth. They somewhat resemble what is seen in subacute yellow atrophy.

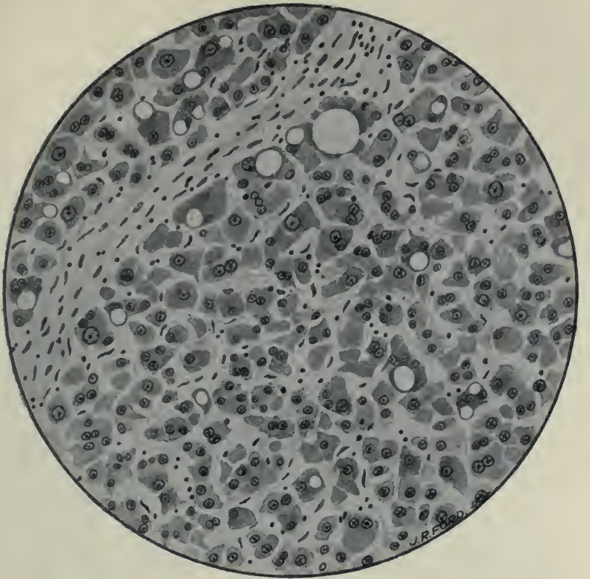


FIG. 4. Section of liver from Case 8, showing slight changes.

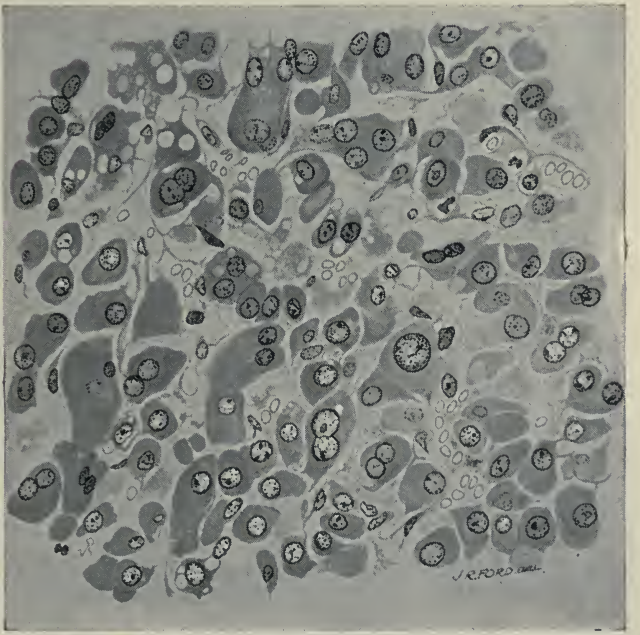


FIG. 5. Section of liver from a case of spirochætal jaundice, showing dislocation of cells and marked degenerative changes.

In very acute cases of short duration (Fig. 6) advanced changes have been found in the liver, both naked-eye and microscopic. In such rapidly fatal infections the organ is diminished in size, with a wrinkled capsule, the section reveals loss of lobular pattern and numerous yellow areas of necrosis. Here complete destruction of liver cells may be seen, the framework of interstitial tissue only being left. Hart and other German workers bear out these earlier observations in the British army.

It would thus appear that the disease falls with varying force on the liver, the changes showing gradations between the slightest deviation from normal structure and an extreme degree of destruction indistinguishable from acute yellow atrophy. Hart describes the subsequent anatomical changes which followed disorganization of the liver in a case which lived three months. The liver had an irregular surface, lobular structure was lost, only islands of liver tissue remained, and there was an extensive fibro-nuclear infiltration round these islands—in other words cirrhosis had supervened on acute atrophy.

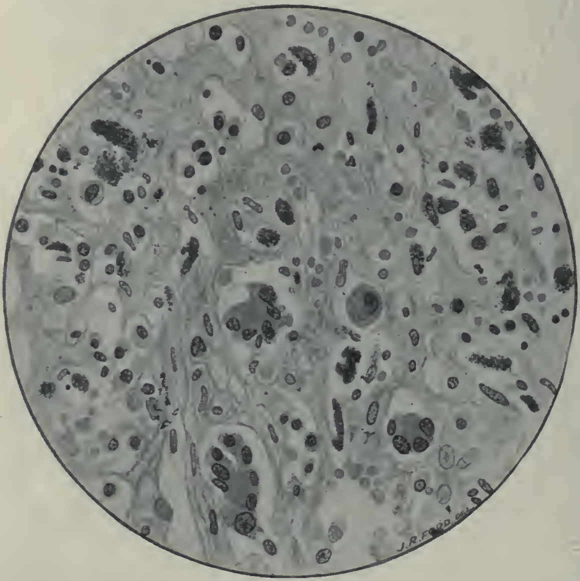


Fig. 6.—Section of liver from a case of spirochætal jaundice showing extreme degrees of change.

The changes in the kidneys likewise vary, though not so much as those in the liver. The appearances (Figs. 7 and 8) may be merely those of cloudy swelling ; there may be infiltration with polymorphonuclear leucocytes between and within the renal tubules ; or there may be in addition hæmorrhages in the glomeruli causing disruption of cells ; the protoplasm of the tubular epithelium may stain badly, have a granular appearance and show vacuolation—in short, the changes may approach those of necrosis

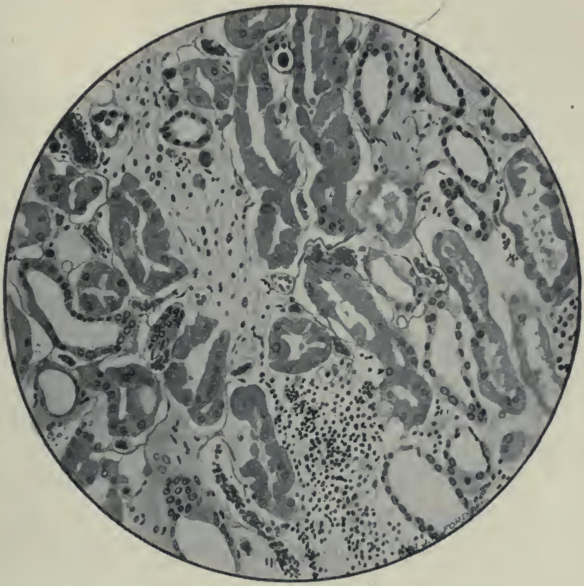


FIG. 7.—Section of kidney from a case of spirochætal jaundice showing cloudy swelling as well as inter- and intra-tubular polymorphonuclear infiltration.

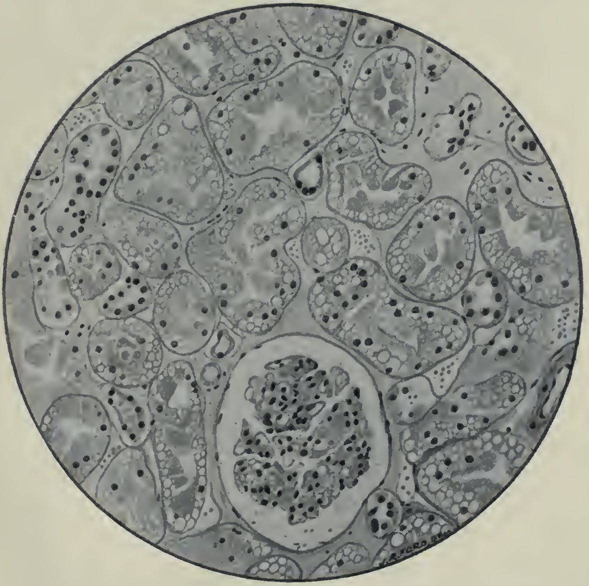


FIG. 8.—Section of kidney from a case of spirochætal jaundice showing marked degenerative changes in the parenchyma.

The spleen and pancreas show no departure from the normal. Peritoneal, subpleural, and sub-pericardial hæmorrhages are often seen. Even more common are hæmorrhages within the substance of the lung, sometimes reaching the size and consistency of the hæmorrhagic infarcts met with in mitral stenosis. In no other organ of the body has anything worthy of note been found.

In the case illustrated in Plate VI the patient died on the eleventh day, having spat up glutinous dark red blood continually for thirty-six hours.

The upper lobe of the lung shows the staining of jaundice and scattered small sub-pleural hæmorrhages. The lower lobe has been sliced open in order to reveal the distribution of the hæmorrhage throughout the substance of the lung. This appearance is very similar to that produced in guinea-pigs experimentally by the injection of blood containing the spirochætes, which has been compared by the Japanese workers, who discovered the nature of the illness, to the mottled wings of a butterfly.

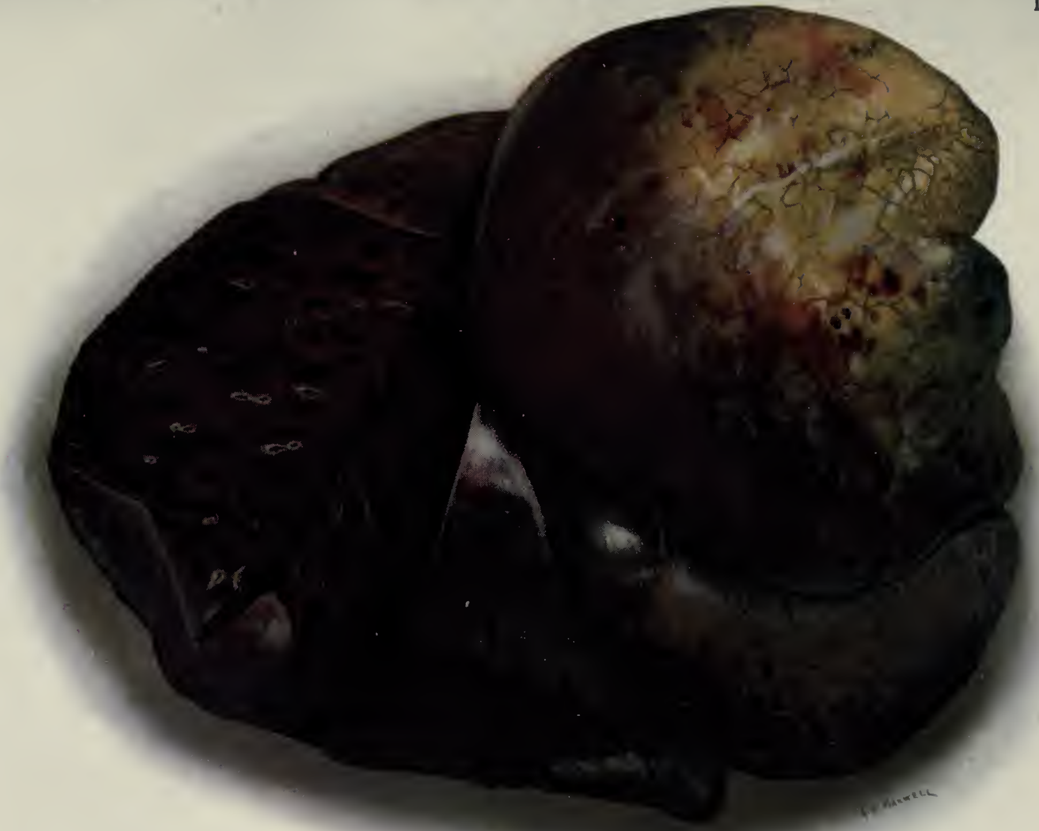
The pathological appearances, like the clinical manifestations, indicate that the brunt of this infection does not always fall on the same organs. When inflammation and swelling of the duodenum and papilla of Vater occur, without any change in the liver beyond bile stasis, the jaundice is clearly due to obstruction at the outlet of the common bile duct. When, on the other hand, as is more common, there is disorganization of the lobules, with damage to the cells and intrahepatic ducts, the jaundice must be due to derangement of secretion within the liver. In the absence of definite changes in the liver and of duodenal inflammation there is no jaundice.

Diagnosis.

A comparison between acute yellow atrophy and spirochætosis icterohæmorrhagica is worthy of attention. On the pathological side two of the illustrations manifest a striking resemblance to acute and subacute yellow atrophy. On the clinical side acute yellow atrophy, though usually running a rapid course, may extend to fourteen or more days' illness. Again, in the wards the clinical picture has often been that of acute atrophy, and yet there have been no characteristic changes in the liver after death. Such cases are described as "icterus gravis," thus avoiding the difficulty in diagnosis. Further, Rolleston records a case of acute yellow atrophy without jaundice.

Onset sudden, with pain and slight hæmatemesis. On second and third days hæmatemesis, and on following three days melæna. On second day liver dullness was diminished. The temperature was usually between 99° and 100° F. No jaundice. The patient became progressively weaker and drowsy, and died on the eighteenth day. *Post mortem* the liver showed acute yellow atrophy.

Plate VI.



RIGHT LUNG FROM A CASE OF SPIROCHÆTAL JAUNDICE (ICTERO-HÆMORRHAGICA).

Spirochætosis ictero-hæmorrhagica may therefore be regarded as a disease in which certain symptoms and lesions can be referred to a definite known cause, and acute yellow atrophy as a provisional term denoting a condition in which the same symptoms and lesions occur but the cause is unknown.

The spirochæte can sometimes be found in the peripheral blood stream of patients suffering from the disease. Injection of infected human blood into the peritoneal cavity of the guinea-pig will, after an incubation of about a week, produce a characteristic fatal illness in that animal, in whose tissues the spirochætes are present in large numbers. The spirochæte has occasionally been isolated in pure culture from the blood, and the guinea-pig inoculated from such culture contracts the disease. The disease has been produced in man by accidental inoculation from an infected guinea-pig. After the first fortnight of the disease the spirochæte may be found in the patient's urine, and in the third week of the disease the patient's serum agglutinates the spirochæte.

At the commencement of the illness there may be difficulty in diagnosis from the fact that the early symptoms may be limited to those common to this and other diseases such as influenza, enteric fever, trench fever or cerebro-spinal meningitis. The complete clinical picture with jaundice is not present until the fourth or fifth day. The occurrence of hæmorrhages will certainly suggest spirochætosis ; the same will be true, though in less degree, of conjunctival suffusion and herpes. Both of these may also occur in trench fever, though the herpes in the latter is not hæmorrhagic.

The guinea-pig test should be carried out the moment that suspicion arises, for the blood of the patient suffering from spirochætosis is only infective during the earlier stages of the disease. After the fifth day the chances of a positive result diminish, and after the eighth day are few. Since the average day of appearance of jaundice is the fourth or fifth, it is easy to see that the opportunity of inoculating a guinea-pig in time may easily slip. Though, therefore, this diagnostic test is conclusive, it has in practice its limitations. In mild cases and non-jaundiced cases these limitations are even greater, for in the former the infectivity of the patient's blood is of more brief duration, and in the latter the manifestations suggesting the presence of this disease will often be too late in appearing.

During the second week of the illness the differentiation of the enteric group will be assisted by the fact that the reaction of the patient to atropine ($^1/_{30}$ gr. hypodermically) is normal, whereas in enteric the acceleration of the pulse is often absent.

A study of the clinical manifestations of the enteric group of diseases during the war will show how closely they can resemble spirochætosis in its earlier stages. The onset of paratyphoid fever was often sudden, there were head and body pains, vomiting was sometimes an early feature, the abdomen was commonly flat and the spleen was frequently not palpable. The occurrence of stupor, hæmorrhage and jaundice would enable a diagnosis to be made.

Between spirochætosis and trench fever in their earlier stages clinical differentiation is often impossible.

After the ninth day, if the disease is spirochætosis, spirochætes appear in the urine, reach their maximum about the fifteenth day and disappear at the end of four or five weeks. Jaundice in typhoid or paratyphoid fever does not usually appear before the end of the second week, that is, a week later than in spirochætosis. Cases of enteric fever do, however, occasionally occur in which jaundice appears early, and the resemblance in the manifestations of the two diseases is then very close. Blackwater fever and bilious remittent fever may both of them be mistaken for spirochætosis. Yellow fever also closely resembles it.

Prognosis.

The Japanese found the mortality of the disease to be 30 per cent. In Europe it has certainly been much less. Stokes and his colleagues observed 100 cases of which six died. Dawson and Hume observed 78 cases of which five died. McNee estimates the mortality as not over four per cent. Death usually occurs from the severity of the disease within the first fortnight, but has occurred at twenty-one days from nephritis, at twenty-eight days, cause not stated, and after three months when extreme atrophy and cirrhosis of the liver were found. The suspicion arises that the foundations of chronic disease of the liver or kidneys may be laid in some patients who recover from the spirochætosis, but as yet there is no definite knowledge on this point.

Treatment.

The Japanese prepared an antitoxic serum, but found little advantage from its use. Pettit and Martin prepared a curative serum from the horse which they found effective in the case of guinea-pigs. This has since been confirmed by Noguchi. Its use in man is doubtful. Renaux and Wilmaers reported in favour of it, and Bassett-Smith recommended that it should be supplied to the naval forces in France, but Garnier found no benefit from its use in thirteen cases. Stokes showed that guinea-pigs infected from rats could be cured from the serum of a convalescent human patient.

EPIDEMIC CATARRHAL JAUNDICE.

Under the titles epidemic catarrhal jaundice of campaigns, epidemic jaundice of campaigns, and camp jaundice, is included a form of jaundice usually slight in degree in which the constitutional symptoms are mild. It has the features of an infection, either a blood infection which has localized in the duodenum, for example, or less often perhaps an infective gastritis which has extended to the duodenum. The usual symptoms are malaise, transient fever, headache, anorexia, nausea, abdominal discomfort, with jaundice supervening later. In France and Flanders these cases of jaundice only occurred singly or in small groups, and not in epidemics as they did in the Eastern theatres of war.

Epidemic catarrhal jaundice broke out in certain camps in Alexandria in July 1915, and thereafter spread rapidly to Gallipoli, Mudros, Salonika, and ultimately to Mesopotamia. Gunson and Gunn described the group of cases occurring at Alexandria among British troops during the summer of that year. Early in 1916 Willcox published an account of epidemic jaundice in the Dardanelles. This paper was supplemented by C. J. Martin's article on the pathology and ætiology of the outbreak and by the bacteriological reports of Archibald, Hadfield, Logan and Campbell, working at the Mudros laboratories.

It was so prevalent as to be an important cause of invaliding. Thus in Helles between 15th October and November 1915, out of a total of 2,062 sick cases, 385 or 18 per cent. were cases of jaundice. The number of cases of jaundice in Helles from 5th September to 6th November was 2,195.

Out of a total of 22,810 sick evacuated from Suvla from 8th August to 7th November, 676 or three per cent. were cases of jaundice; and a large number were treated in the field ambulances. Between 12th August and 1st December the number of cases in the three field ambulances of the 53rd Division in Suvla was 456 as compared with 612 cases of "pyrexia" and 4,026 cases of dysentery and diarrhœa. Its rate of incidence and relation to the above-mentioned conditions are shown in the following tables.

Number of cases of Dysentery and Diarrhœa, Pyrexia and Jaundice evacuated from Suvla Bay.

Week ending	Diarrhœa and Dysentery.	Pyrexia.	Jaundice.
August 15, 1915	161	5	—
,, 22 ,,	339	16	—
,, 29 ,,	913	101	8
Sept. 5 ,,	840	58	4
,, 12 ,,	827	147	7
,, 19 ,,	1080	189	17
,, 26 ,,	1037	178	17
Oct. 3 ,,	1144	309	38
,, 10 ,,	971	242	52
,, 17 ,,	790	154	123
,, 24 ,,	922	206	109
,, 31 ,,	875	251	169
Nov. 7 ,,	621	282	132
Total	10,520	2,138	676

Incidence of Dysentery and Diarrhœa, Pyrexia and Jaundice, in 53rd Division, Suvla Bay.

Week ending	Diarrhœa and Dysentery.	Pyrexia.	Jaundice.
August 19, 1915	441	1	—
,, 26 ,,	354	2	5
Sept. 2 ,,	544	14	1
,, 9 ,,	326	47	—
,, 16 ,,	256	60	—
,, 23 ,,	237	58	2
,, 30 ,,	224	48	—
Oct. 7 ,,	229	48	3
,, 14 ,,	201	62	10
,, 21 ,,	292	66	20
,, 28 ,,	206	35	51
Nov. 4 ,,	172	37	70
,, 11 ,,	154	57	72
,, 18 ,,	225	32	61
,, 25 ,,	120	24	103
Dec. 1 ,,	45	21	58
Total	4,026	612	456

Between 24th September and 31st October the number of cases admitted into the field ambulances of the 13th Division at Suvla was 74; in November it rose to 287 and then fell to 92 by 19th December when Suvla was evacuated—a total of 453 cases. Similar rates of incidence occurred in every unit on the Gallipoli Peninsula.

On evacuation of the Peninsula in December 1915, jaundice from Suvla Bay was brought back to Egypt by the 53rd Division, but it rapidly died out by the end of January 1916.

It was carried by the 10th Division from Suvla Bay to Salonika in November 1915, and prevailed in that division during the intensely wet weather in December, high up on the Bulgarian mountains. Cases of jaundice there constituted a third or more of the total sick admitted into hospitals in December 1915. It then died out and did not reappear.

The 13th Division which had also been badly affected in Suvla Bay returned to Egypt for the first three months of 1916, and afterwards went to Mesopotamia carrying the infection with it, for a sharp outbreak of 555 cases occurred in this division in June 1916. The incidence fell rapidly during July and August.

The usual history in any battalion affected commenced with one or two isolated cases; then there was an interval of about three or four weeks with an occasional case; then a large number of cases for three weeks; and finally an occasional case for a few more weeks.

Ætiology.

The epidemic character of the disease in the Dardanelles and Mesopotamia was beyond doubt. There were numerous instances of a large proportion of the cases occurring in one unit. In general, infection appeared to be due to a common cause, though cases occurred in which it appeared to be conveyed from person to person. There was close association between the incidence of epidemic jaundice and that of the dysentery and enterocolitis groups of affections. The charts of the two groups showed that the jaundice curve reached its summit about three weeks after the dysentery curve. Moreover, a recent history of diarrhœa was not uncommon in the jaundice cases. On the other hand, no jaundice occurred in Gallipoli till early in August, although dysentery and diarrhœa were very prevalent from June onwards.

Bacteriological investigation of epidemic catarrhal jaundice was carried on with great persistence by many observers. Cases here and there were found in which an organism of the enteric group, typhosus or paratyphosus, was present. Spirochætal infection as a cause was definitely excluded in those cases which were studied after the recognition of spirochætosis icterohæmorrhagica. Blood and urine cultures yielded no results. Mackie found an organism of *B. coli communis* type during life on two occasions—once from liver puncture and once from the urine.

In one case where duodenal intubation was tried, Martin and Hurst, in Mudros, obtained a bacillus of the fæcalis alkaligenes group in six out of eight cases, and in three out of four control cases.

The typhoid-coli group of organisms produces many varieties of infection, the clinical manifestations of which are only very imperfectly determined. In the war there were infections whose symptoms did not conform to atypical paratyphoid fever.

The facts point to this epidemic catarrhal jaundice being due to an infection which is localized in the upper part of the alimentary tract, but the actual organism is unknown.

Observation suggests that the incubation period of the infection is at least two weeks, and according to Hunter in most cases even more. The uniformity in its mode of incidence and its subsequent spread is of importance in connection with the question of its ætiology, namely, whether it is only an incidental complication of other known infections, *e.g.*, typhoid, paratyphoid, or dysentery, or on the other hand an infection *sui generis*. Taken as a whole the facts speak for the specificity of the infection.

Symptoms.

The clinical picture appears to have been fairly constant. The illness was, as a rule, ushered in with headache, general malaise, loss of appetite, fever, nausea, and sometimes vomiting, with discomfort and tenderness over the upper abdomen. The abdominal symptoms would sometimes precede the onset of pyrexia. Constipation was as common as diarrhœa. The tongue was usually furred but in some cases remained clean.

Jaundice appeared on the third or fourth day of illness, sometimes with the decline of pyrexia ; it reached its height about the tenth day and then gradually faded. It varied much, however, in intensity and duration ; when severe it was liable to last several weeks, but it seldom ran parallel with the malaise. The jaundice was sometimes associated with swelling and tenderness of the liver and less often of the gall-bladder, and with enlargement of the spleen (Chart VI).

In Mesopotamia, Willcox frequently observed that about the third or fourth day precordial dullness increased on the right side. This increase lasted only for four or five days and then subsided. During the fever the pulse quickened to 80 or 90, but in some cases it was noticed that it was only 50 when jaundice commenced. The urine contained bile, and slight albuminuria was not unusual. The stools were clay-coloured. Persistent pain in the back and legs was a feature of some cases.

There was a liability to relapses of four or five days' duration. Many patients suffered from persistent weakness accompanied often by a marked loss of weight. Convalescence lasted two or three months.

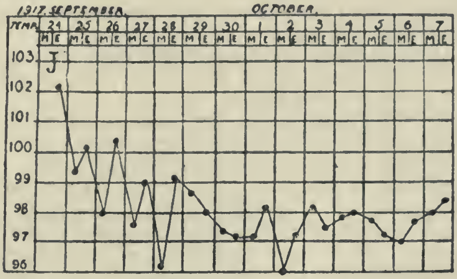
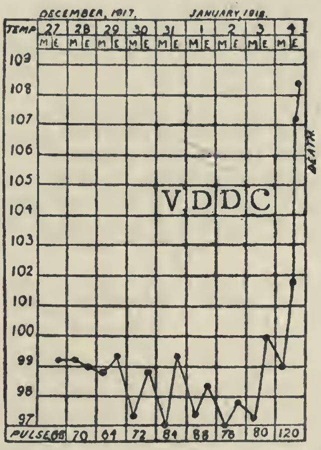


Chart VI.—Epidemic Catarrhal Jaundice.

Jaundice appeared on 24th September. On 26th September liver and spleen enlarged and right heart dilated (Willcox).

Generally speaking, infective catarrhal jaundice, both in the sporadic and epidemic forms, was a mild though somewhat exhausting illness. Here and there, however, more severe infections occurred, and sometimes what appeared to be a typically mild case passed on to icterus gravis and ended fatally. During the jaundice stage acute toxic symptoms developed and death ensued two or three days after their onset.



V = Vomited.
D = Delirious.
C = Coma.

Post-mortem, pale yellow atrophy.

Chart VII.—Epidemic Catarrhal Jaundice with Icterus Gravis. Jaundice before Admission.

The grave symptoms usually supervened about ten days after the first appearance of the jaundice, though in one case they developed as early as two days, and in another as late as twenty-nine days. There was no foreboding of these grave developments in such cases. The following case illustrates this occurrence (Chart VII).

Patient taken ill 24th December, 1917, with slight fever and usual symptoms of epidemic catarrhal jaundice. On 28th December, temperature normal, liver enlarged and tender, spleen palpable and slightly tender, tongue furred, constipated, definitely jaundiced, urine bile-stained, mental condition normal. Several attacks of vomiting, with no blood, occurred during the next three days.

2nd January, 1918:—Vomit contained streaks of blood and was bile-stained. Jaundice now deep. Very restless and maniacal during last night and this morning.

3rd January, 1918:—Vomit as on previous day. Epistaxis in morning, liver dulness much diminished, being only two inches vertically; knee jerks increased. Very restless and noisy.

4th January, 1918:—Patient became comatose in morning, urine contained albumen, bile, and a few red corpuscles, no spirochætes found in urine or blood.

5 p.m.—Cheyne Stokes breathing, extensor plantar reflex.

10 p.m.—Temperature suddenly rose to 109°, death occurring at 10.30.

Post-mortem Examination.—Liver 39½ ozs. stained yellow. Spleen enlarged and soft, kidneys yellowish. Small hæmorrhages in pleura, pericardium, omentum, mesentery, and lungs. Wall of stomach and duodenum contained petechiæ and contents were blood-stained.

Microscopical examination and animal experiments for spirochætes of liver, kidney, and spleen were negative. Liver showed almost complete destruction of hepatic cells in blocks, only isolated islets of cells remained, in parts total necrosis of all but trabecular tissue. Kidney, extensive degeneration of tubular cells. Pancreas, early but definite cell necrosis, with shrinkage and loss of outline of the cells that remain, in some places great reduction in number of cells.

The following case is an example of a more severe infection from the outset.

Onset was gradual with chilliness, fever, weakness, anorexia, abdominal pain and vomiting. On the fourth day, patient declared sick, and the temperature was 108°. On the fifth day the temperature was normal and jaundice appeared. The upper half of the abdomen was tender and the spleen could be felt for 1½ inches below the costal margin. The jaundice rapidly became deep, but, though apathetic, the patient never was in a toxic condition. The urine contained bile and a trace of albumin.

On the ninth day the jaundice was slightly less. On the tenth day there was a return of fever and the spleen remained palpable, but there was no deepening of the icterus. The temperature did not finally settle till the eighteenth day; the jaundice and the enlargement of the spleen had disappeared on the twentieth day, and by that time convalescence was established.

The atropin test was made twice—on the sixth day, when there was an escape of 20 (60-80), and on the fifteenth day, when there was an escape of 16 (66-82).

Agglutinations were tested three times—on the ninth, fourteenth and nineteenth days. They were negative to paratyphoid A and B, and typhoid remained constant at 1 in 215. The patient had been inoculated against typhoid only two years previously.

A blood culture was made during a relapse of fever, and two cultures from urine and two from fæces were negative to the enteric group. On two occasions the urine was thoroughly searched for spirochætes, but with negative results.

The fasting stomach and duodenum were intubated. Cultures from the gastric contents were negative, while those from the duodenum contents showed a growth of a gram negative coccobacillus. The characters of this bacillus were tested by putting it through broth, gelatine, agar, litmus milk, litmus whey, peptone, and the sugars. Litmus milk and whey became alkaline in twenty-four hours without clot formation in the former. The sugars were not acted upon, with the exception of glucose, from which acid without gas was formed after forty-eight hours' incubation.

This coliform organism was the sole positive result from the investigations. It was not agglutinated by the patient's own serum.

JAUNDICE IN THE ENTERIC GROUP OF FEVERS.

Jaundice is an uncommon though interesting feature of enteric fever. During the first two and a half years of the war its incidence among cases of enteric in the British armies in France and Flanders was 1·38 per cent., and amongst cases occurring at the Dardanelles and in Mesopotamia, according to Willcox, as much as 5 per cent. The jaundice may occur early in the illness, that is, before the tenth day, or during the later stages; it may present every grade from faint to deep pigmentation. If severe, the icterus will make the patient more drowsy and toxic, otherwise it seems to have little effect on the course of the illness and its appearance in the later weeks is not necessarily associated with either return of fever or exacerbation of symptoms. Of the early symptoms, headache is the most constant, and vomiting is common. In a series of 26 cases the following were the manifestations with their relative frequency: headache 19, vomiting 12, abdominal pains 8, back and leg pains 8, diarrhœa 5, shivering 2, extreme lassitude 2, epistaxis 1. Spots were present in four cases, and the spleen was palpable in four cases, but the relative infrequency of these two manifestations, as also of abdominal distension, was characteristic of the clinical picture of enteric fever in France and Flanders throughout the war. When the jaundice occurred early its onset was more often sudden, whereas when it occurred at a later stage a gradual onset was more usual.

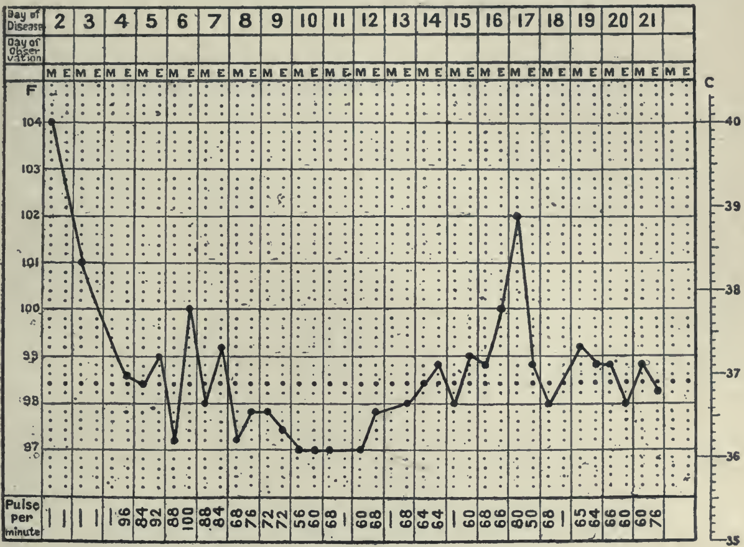


Chart VIII.

When jaundice occurs early in a febrile illness, the possibility of one of the enteric groups being the underlying cause may easily escape notice, and this is especially the case if the fever is of short duration, or moderate in degree, as is illustrated by the following case of infection by *B. typhosus* (Chart VIII).

There was a sudden onset with extreme lassitude and headache, which forced the patient to bed within a few hours. On the second day there were pains in the head, legs and across the abdomen, and the temperature was 104°. On the fifth day there was repeated vomiting, and icterus, which had shown itself on the previous day, had become definite. By the sixth day the jaundice was marked, though the temperature had fallen and the pulse-rate was 88; the abdomen was flat, but tender in its upper half; the spleen was not enlarged, but the liver extended three fingers' breadth below the costal margin; no herpes; the glands were shotty; the patient was apathetic and drowsy. The next day the apathy continued and there was vomiting. On the eighth day the white cells were 23,800 per c.mm., the red cells 4,800,000 and the hæmoglobin was 80 per cent. Films showed the red cells to be normal. On the tenth day there was still apathy, the tongue was dry in the centre and furred at the side, the spleen was enlarged to percussion, but not palpable; the urine had a specific gravity of 1,011, was acid, contained bile and numerous hyaline and granular casts, a few red blood cells, but no albumin. The casts had disappeared two days later and a trace of albumin had appeared.

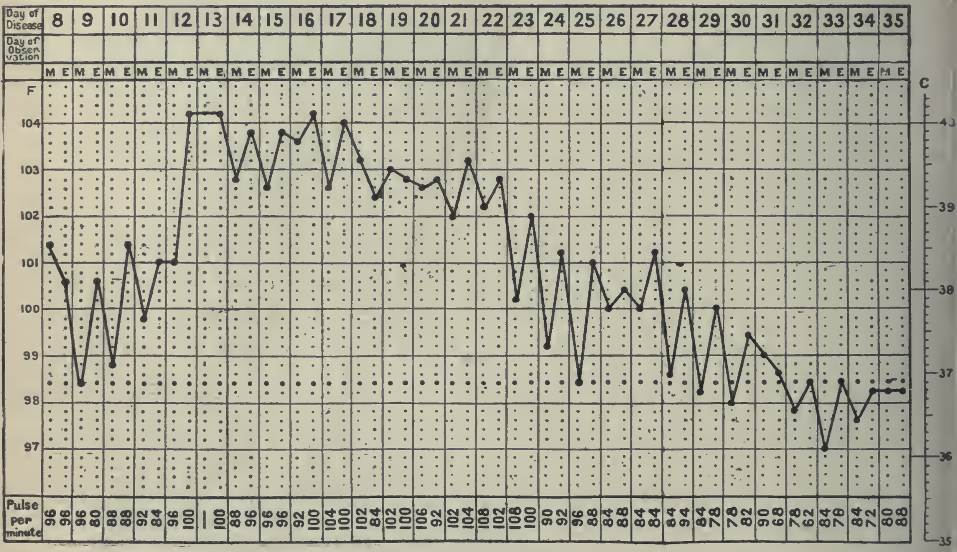


CHART IX.

On the fifteenth day the patient's condition had improved; the jaundice, though still marked, was diminishing; the spleen, however, had become distinctly palpable. Blood pressure was 118 systolic and 58 diastolic. In spite of a slight rise of temperature on the seventeenth day the patient's condition steadily improved, and the jaundice faded.

On the tenth day after the injection of $\frac{1}{30}$ grain of atropin, the maximum acceleration of the heart was only six beats (70 to 76) in 50 minutes. On the sixteenth day the same dose of atropin produced an escape of twenty-four beats (68 to 92) in half an hour. The difference in these two observations illustrates what Captain Marris has pointed out—that the locking of the heart under atropin in the enteric group may be limited to a few days, the favourite period being about the tenth day.

Bacteriological cultures from the blood, stool and urine were negative. Agglutinations on the eighth day showed a big rise in typhoid, viz., 1 in 2,500, rising after delay to 1 in 3,675. On the sixteenth day the agglutinations had fallen to 1 in 2,822. Paratyphoid A and B were negative to 1 in 5. The patient had been inoculated against typhoid about a year previously but not against paratyphoid.

Investigation was made for spirochætosis ; a guinea-pig was injected with the patient's blood on the sixth day, but with negative results ; the urine was examined twice for spirochætes, the last time on the seventeenth day, and with negative results.

This is a case of interest, for it might easily have been mistaken for either spirochætal or catarrhal jaundice. The acute onset, lassitude and pains, the jaundice developing as the temperature fell, the shotty glands, could justly have pointed to spirochætosis ; and if the atropin test had not been applied till the sixteenth day, the escape of the heart might have been an argument against enteric fever. On the other hand, the very brief period of fever, the flat abdomen, and the absence of splenic enlargement in the early part of the illness might well have led to a diagnosis of catarrhal jaundice.

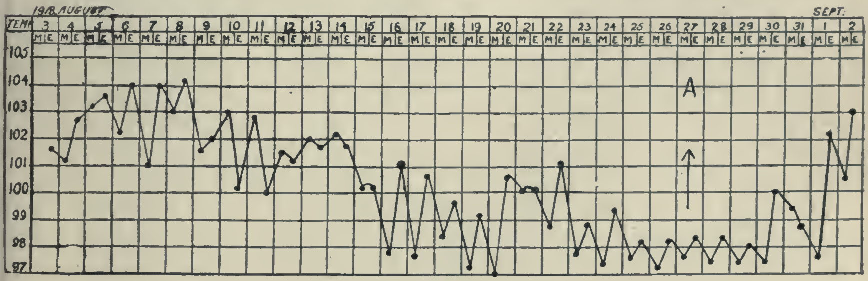


Chart X.

Chart IX represents the chart of a case of infection by *paratyphosus B*. Here again the onset was sudden, the patient being seized with pains in the legs, which were so bad that he was unable to stand. Later he vomited. At the onset of the illness the temperature reached 104°. On the third day jaundice appeared in the conjunctivæ and rapidly spread all over the body. On the eighth day the temperature was 101·2° and the pulse rate 96 ; the patient was deeply jaundiced and drowsy and complained of a general aching The liver extended three fingers' breadth below the ribs ; the spleen could not be felt, but the splenic region was very tender.

On the twelfth day the temperature rose further, and the patient became worse. On this day the atropin test was applied, and after the injection of $\frac{1}{30}$ grain the heart only quickened four beats, from 100 to 104. He was more drowsy ; there were bronchitic râles throughout both lungs and the pulse was markedly dicrotic. He remained very ill for three weeks, during which he passed through a serious relapse, associated at its commencement with an increase in the jaundice.

About the twenty-first day the jaundice began to diminish and the symptoms to improve, and at the end of five weeks of illness convalescence was established.

Chart X represents the chart from a case of paratyphoid A in which the jaundice appeared on the sixth day. Paratyphoid A was recovered from the stools.

Such cases indicate the importance of being on one's guard lest catarrhal jaundice is not in reality disguising enteric fever.

When jaundice occurs late in a case of enteric fever there is seldom any added difficulty of diagnosis owing to its presence. The jaundice appears without special symptoms, though, exceptionally, these are suggestive of cholecystitis. Thus, in a case of paratyphoid B, during the fourth week, there were three rigors, jaundice appeared, and the region of the gall bladder became tender. *Bacillus paratyphosus B* was found in a stool, and the agglutination curve pointed to that organism.

Pathology.

The cause of the jaundice in these cases would seem to be some obstruction in the biliary tract. The symptoms are not usually severe or lasting enough for there to be any involvement of the smaller ducts within the liver, and are best explained by swelling of the papilla of Vater as part of a duodenal inflammation due to the localization of the infection in the duodenum. The localization of typhoid and paratyphoid infections, though showing a strong selectiveness for the ileum and colon, does not limit itself always to that part of the intestine, and the lesions may rarely be found not in the intestine at all, but in some other organ—for example, abscess of the spleen.

In a case which occurred in the Dardanelles, jaundice developed on the third day and death occurred on the ninth day. The duodenum was found to be of a velvety appearance and the walls of the common bile duct and hepatic ducts showed acute inflammation. *Paratyphosus B* was recovered from the bile in the gall bladder. This was clearly an ascending inflammation from the duodenum.

On the other hand, Brulé argues that the classical explanation of the origin of jaundice—namely, that there is a mechanical obstruction of the larger or smaller bile ducts, or of both—is not wholly satisfactory in the light of modern investigations. He seeks to prove that in view of the infective origin of most cases of jaundice, excluding those caused by gross obstructions of bile ducts, the biliary retention must be due to a hepatitis rather than to angiocholitis, and that the derangement of secretion must occur in the liver cells themselves. His work as a whole throws some new light on the problems of hepatic disease. Holding that injury of the secretory cells of the liver is the usual cause of jaundice, he believes that jaundice caused by obstruction of the bile ducts is relatively uncommon.

Jaundice associated with pylephlebitis may very rarely be caused by infection due to one of the enteric group of organisms, and one such case occurred in France.

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CHAPTER XVIII.

SCURVY.

SCURVY is defined as a disorder of metabolism due to deficiency of a certain accessory food factor or vitamine present in fresh food such as vegetables, fruits and meat. It is characterized by great debility, anæmia, special changes in the gums and a tendency to hæmorrhage. The history of scurvy during the war and the knowledge gained from a practical study of the disease in the various epidemics which occurred, together with the recent experimental study of the effect of diets which produce scurvy in animals, place it with certainty in the group of deficiency diseases.

By far the greatest incidence of scurvy during the war occurred in Mesopotamia, where, in 1916, a very severe epidemic occurred amongst the Indian troops. During the years 1916, 1917 and 1918 the following number of admissions and deaths were recorded amongst them :—

	Admissions.	Deaths.
1916. July 1st to December 31st ..	11,455	24
1917. Jan. 1st to December 31st ..	2,199	6
1918. Jan. 1st to November 30th ..	825	2

A very large number of cases occurred in the first half of 1916, but statistics of these are not available.

The great incidence of scurvy is explained by three factors :—

(1) The ration scales of Indian troops which were in force until July 4th, 1916.

(2) The system of rationing Indian troops in stations in India prior to 1917. Under this system the Indian soldier received a money allowance in lieu of rations, and he bought his food from the bunniah or food contractor of his unit. There was thus no guarantee that he consumed the equivalent of a service ration. As a consequence of this system a considerable percentage of Indian troops arriving in Mesopotamia from India were anæmic, debilitated and suffering from pyorrhœa. With men in this condition the latent period for scurvy would be short were dietetic deficiencies imposed upon them.

(3) The military situation in Mesopotamia up to March 1917.

Until the occupation of Baghdad, on 11th March, 1917, the troops in the fighting area were stationed in districts far from centres of native population, and local supplies of fresh vegetables or fruit were unobtainable. At Basrah and Amara a certain amount of fresh vegetables and fruit was grown, but not in sufficient quantity to supply troops in the fighting area. It is interesting to note, however, that in Indian troops stationed at Basrah and Amara the scurvy incidence was very much less than amongst troops at the front, since antiscorbutic foods were available for them to some extent from native sources.

Added to the absence of adequate local supplies of suitable foods there was great difficulty of transport. Between 28th September, 1915, when the force had advanced to Kut, and 23rd February, 1917, the front area of operations was some 300 miles by river from Basrah. During this period all supplies had to be sent by river transport, and owing to the intense heat during the summer months it was impossible to convey fresh vegetables and fruit to troops in the front area, since supplies of these articles, when sent, invariably arrived in a damaged condition and unfit for human consumption. There was not then available special river transport, such as refrigerating barges, for the conveyance of these perishable articles, so that there was a great deficiency, indeed almost a complete absence, of the food stuffs rich in antiscorbutic vitamine in the rations issued to troops in the front area.

As a consequence of this the experiment was perforce made of feeding a large number of troops on a dietary greatly deficient in the accessory food factor necessary for the prevention of scurvy. The result was a great outbreak of scurvy amongst the Indian troops, while British troops escaped. The explanation of the freedom of the British troops from scurvy is to be found in the much more liberal allowance of fresh meat which was obtainable from local sources. Certain classes of Indian troops, partly from their caste objection to meat and partly from inadequacy of supplies, obtained very little fresh meat during this period. Cases also occurred during the siege of Kut, when the besieged were in straits for food. Minor outbreaks occurred later, especially amongst labour detachments and Hindu non-meat eaters. In most cases they were attributed to insufficient disciplinary action being taken to ensure that the men consumed sufficient antiscorbutic elements in their rations. Strict supervision was maintained by the medical services, and these minor outbreaks and their causes were at once brought to notice.

A number of cases of severe scurvy also occurred during the Dardanelles Campaign at Mudros amongst Indian soldiers who had been serving on the Gallipoli peninsula, and were attached to Indian Mountain Batteries operating there. The ætiological conditions were similar to those of Mesopotamia. A few cases were also seen in Turkish prisoners arriving at Mudros who had been captured at Gallipoli.

In March 1915 three cases of scurvy in Indians were admitted to hospital in Marseilles; two of them had been in France over five months, the third had arrived only a month previously. During April 1915 seven further cases were reported amongst Indian troops in the Marseilles area. All of them, except one, had been in France over six months, and no particular camp was affected, nor could any common factor be discovered. The daily dietary for Indian troops contained, as antiscorbutics, four ounces of fresh meat and two ounces of potatoes, and it seemed probable that the few cases affected had not consumed their full ration of meat and potatoes, and had not supplemented their rations by the purchase of fresh vegetables.

In April 1915 a few cases of scurvy were reported amongst Indian troops in the Indian Corps attached to the 1st Army in France. The Director of Medical Services of the army then issued an order warning medical officers of the importance of early recognition of cases, and advising as regards dietetic prophylactic measures. No further cases were reported.

In June 1918 special attention was paid to the occurrence of scurvy amongst the South African Native Labour Corps Contingent serving in France. A few cases had been reported as early as October 1917, but it was not until May 1918, that the cases occurred in sufficient number to attract attention. In May 1918, out of a strength of 6,795, 121 cases of scurvy were admitted to hospital and a slightly larger number in June 1918. A special investigation was made by the Adviser in Pathology and the A.D.M.S. (Sanitation), as a result of which it was concluded that overcooking of the food and consequent destruction of the antiscorbutic principles was probably the chief cause. It was also suggested that the flour meal supplied, which was different from the native meal to which the men had been accustomed, was a factor, but there was no proof of this. The dietetic measures adopted resulted in the speedy disappearance of scurvy amongst the contingent.

In August 1915 twelve cases in British troops were reported from No. 24 Field Ambulance, 8th Division, as suffering from scorbutic symptoms. These were of a mild type and did not show the characteristic gum changes. Night blindness was a symptom in 10 of these cases, and some had ecchymoses. The symptoms of scurvy were somewhat indefinite, and other cases were not reported.

Only four cases occurred amongst the British troops in North Russia in 1919. Three of them were admitted to hospital suffering from other diseases and developed symptoms of scurvy, apparently as a result of several months' hospital diet. Scurvy amongst British troops in Russia in 1919 may therefore be regarded as practically non-existent, but the reason for the absence of this disease is undoubtedly due to the careful prophylactic measures taken in the light of recent knowledge on the subject.

In February 1919 scurvy was first diagnosed amongst Russian prisoners, and later a large number of severe cases occurred. Captain A. J. Stevenson, who investigated this outbreak, attributed the cause to vitamine deficiency in the prison dietary and to over-cooking of the food.

The average period between the commencement of the prison diet and the development of symptoms was somewhat over four and a half months, but in many cases which had associated diseases the prescorbutic period was less than three months, and some cases, suffering from such diseases as typhus or enteric group disease, developed scurvy in conjunction with these diseases.

A large number of cases was also reported from Murmansk amongst the civil population in March 1919, and measures were taken by the British military authorities to deal with them as far as possible.

Scurvy occurred only to a slight extent amongst native carriers and porters attached to the force in East Africa. Very few cases appear to have occurred amongst the troops. In this connection the following extract from a report to the War Office by Surgeon-General Pike and Lieut.-Colonel Andrew Balfour, who had been specially appointed to report on medical conditions during the East African campaign, is of special interest :—

"During our tour of inspection only one case of genuine scurvy was seen, and such evidence as is available does not point to there having been anything like an outbreak of the disease. Indeed, it would seem to have been uncommon even in the case of Indian troops. This is somewhat remarkable, considering the shortages in food and the lack of anti-scorbutic substances in the Indian dietary. Doubtless cases have been missed or not reported, but, even so, it is strange that in the non-meat-eating units at least scurvy did not make its appearance to any extent. The disease has occurred to a slight extent amongst the carriers. The officer commanding Native Detail Hospital, Dar-es-Salaam, informed us that he had seen cases amongst porters coming from the Rufiji line at a time of great privation and suffering, and it is possible that there were others of which we have no record, for scurvy is not a disease familiar to many medical officers serving in this country.

" A full and careful inquiry into the matter would be both interesting and instructive, but would occupy much time and would have to be carried out as a special research. The fact that there has usually been a fresh meat ration available probably accounts for the absence of scurvy amongst white troops. An inspection of some Indian troops for the presence of pyorrhœa did not indicate that this condition was common amongst them."

On 5th June, 1917, unexplained ecchymoses were observed amongst the German prisoners of war on the island of Raasay in Scotland, and on 6th July, 1917, the diagnosis of scurvy was established. On 22nd August, 1917, Professor Leonard Hill* visited the Prisoners of War Camp and made a thorough investigation of the cause of the outbreak. It appeared that on 24th April, 1917, a somewhat restricted ration scale was introduced from which potatoes were excluded. From this date also the purchase of food by the prisoners was forbidden owing to the food shortage throughout the country. Previously the men had been in the habit of buying from local sources bacon, which they ate raw, and also other articles of food were purchased with the money earned by their work, and the rations thereby supplemented. The onset of symptoms of scurvy occurred about seven weeks after the restriction of the rations, and most of the prisoners affected were those doing work in the mines which was of a somewhat heavy character. The examination of the diet scales showed that, as regards protein, fat and carbohydrates value, and also as regards vitamine content and calorie value, there was an adequate allowance. The figures corresponded to those for the ration scales of English civil prisons, and were equal to those of the German army ration 1916–1917. The values were higher than those of German munition workers and of some hostels and canteens of munition workers in this country. Professor Hill consequently attributed the occurrence of scurvy in the camp not to a deficiency of the rations, but to the method of cooking them, which consisted in stewing the meat and vegetables at about 100° C. for the long period of five hours, whereby the special vitamines would be destroyed. An additional allowance of potatoes and cabbage was made to the ration scales, and precautions were taken against prolonged cooking, following which the outbreak of scurvy, which had not been severe in type, very rapidly cleared up.

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During the war a few cases of scurvy occurred amongst the civil population in England and Scotland in 1917, in certain of the large centres of population such as Manchester, Newcastle and Glasgow, owing probably to a temporary shortage of fresh vegetables, especially potatoes, in addition to the restricted ration of fresh meat.

The attention paid to the increased production of potatoes throughout the country was followed by a disappearance of scurvy.

Ætiology.

It has been conclusively proved that the essential cause of scurvy is the continued absence, over a long period, of an accessory food substance or vitamine in food consumed.

The former theories that scurvy was primarily due to a deficiency of potassium salts, or to an acid intoxication, or to toxic materials in the foods as the result of decomposition, or to a specific bacterial infection must, in the light of recent knowledge, be abandoned.

The antiscorbutic vitamine is contained in a number of fresh foods—in largest amount in oranges, lemons, tomatoes and fresh green vegetables, in considerable amount in roots and tubers such as onions, swedes, turnips, potatoes, and in small quantities in fresh meat and milk. The vitamine is thermolabile and is destroyed by prolonged heating such as stewing. Boiling for a short period is less destructive than prolonged heating at a slightly lower temperature such as occurs in stewing. It is also rapidly destroyed by alkalies such as carbonate of soda, which should not be used in the cooking of vegetables. Desiccation causes destruction of the antiscorbutic vitamine so that it is absent from dried food stuffs.

Cabbage cooked for one hour at temperature ranging from 80° to 100° C. loses about 90 per cent. of its original antiscorbutic value. Heating in water for sixty minutes at 60° C. or for twenty minutes at 90° to 100° C. causes similarly a loss of about 80 per cent.

Freezing reduces the amount of antiscorbutic vitamine so that frozen meat contains less than fresh meat.

The history of scurvy in Mesopotamia furnishes a good example of the effect of a dietary deficient in antiscorbutic vitamine. Up to 4th July, 1916, the rations of the troops in Mesopotamia were the field service rations given in Tables I and II of "War Establishments, India," 1916.

TABLE I.

Field Ration of British Troops.

Bread	1 lb.	Sugar	2½ oz.
Fresh meat	1 lb.	Salt	½ oz.
Bacon	3 oz.	Pepper	1/36 oz.
Potatoes	1 lb.	Fuel	3 lb.
Tea	1 oz.		

Extras.

Chocolate	1 oz.
or Bread	4 oz.
Lime Juice	½ oz.
or Sugar	½ oz.
Rum	4 oz.

TABLE II.

Field Ration of Indian Troops and followers.

Atta	1½ lb.	Ginger	⅓ oz.
Fresh meat	4 oz.	Chillies	⅙ oz.
Dhall*	4 oz.	Turmeric	⅙ oz.
Ghi	2 oz.	Garlic	⅙ oz.
Gur	1 oz.	Salt	½ oz.
Potatoes	2 oz.	Fuel	1½ lb.
Tea	⅓ oz.		

Extras.

Atta	½ lb.	Rum	2 oz.
Ghi or Gur	1 oz.	Lime Juice and sugar	½ oz. of each.

It is seen from these ration scales that the ration of the British soldier was protective against scurvy, while the Indian ration was very greatly deficient in antiscorbutic vitamine, the only substances containing this being potatoes 2 oz., and fresh meat 4 oz.

As mentioned above, owing to difficulties of transport, even these two items were commonly absent from the ration actually issued to Indian troops at the front. The result was a great outbreak of scurvy in 1916, which began to subside in November 1916, as a result of the improved rationing of the troops.

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* Dhall is the name given to the dried whole or split edible seed of several varieties of Leguminosæ occurring in India. It has formed part of the ration for Indian troops and is liked by them. It is equivalent to small dry lentils.

British troops were immune from scurvy in Mesopotamia, the few isolated cases which occurred among them being due to a restriction of dietary made necessary by some other disease occurring in the individual patient.

The importance of an addition of antiscorbutic articles to the Indian ration was fully realised by the director of medical services, who strongly represented the necessity of an improvement as regards protection against scurvy. On July 4th, 1916, new ration scales were consequently sanctioned in which the addition was made to the Indian ration of the antiscorbutics, fresh fruit 2 oz., and as extras, fresh fruit 4 oz., fresh vegetables 4 oz., fresh meat 2 oz., tamarind 2 oz.

The revised field ration of Indian troops then consisted of the following articles :—

Atta	1½ lb.	Condensed milk	2 oz.
Fresh meat	4 oz.	Tea	⅛ oz.
Dhall	4 oz.	Ginger	⅓ oz.
Ghi	2 oz.	Chillies	⅙ oz.
Gur	2 oz.	Turmeric	⅙ oz.
Potatoes	2 oz.	Garlic	⅙ oz.
Fresh fruit	2 oz.	Salt	½ oz.
Tobacco (weekly)	2 oz.	Fuel	1½ lb.
Matches (boxes, weekly)	2		

(Substitutes same as for British troops.)

Extras.

Atta	½ lb.	Fresh fruit	4 oz.
Ghi 1 oz. or Gur	2 oz.	Tamarind	2 oz.
Fresh meat	2 oz.	Rum (25 per cent. under proof)	2 fl. oz.
Fresh vegetables	4 oz.		

In August 1916 the Medical Advisory Committee appointed by the War Office visited Mesopotamia. The occurrence of scurvy in the force received special attention and investigation, and on 31st October, 1916, the ration scales were further improved. The rations for Indian troops then became :—

Daily.

Atta or Rice	1½ lb.
Fresh meat	6 oz.
Gur (when fresh meat not obtainable)	2 oz.
Dhall	4 oz.
Gur	2 oz.
Ghi	2 oz.
Potatoes or fresh vegetables	6 oz.
Dried vegetables (when fresh not available)	2 oz.
Fresh fruit	2 oz.
Tinned fruit 2 oz. or dried fruit 1 oz. (when fresh fruit not available.)	
Tea	⅓ oz.
Milk, tinned	2 oz.
Condiments (ginger, chillies, garlic, turmeric)	¾ oz.
Salt	½ oz.
Tamarind or cocum	2 oz.
Fuel (wood)	2 lb.

Thrice weekly.

Ghi (Mondays, Wednesdays, Fridays)	2 oz.
Lime juice (Tuesdays, Thursdays and Saturdays, not in winter)	½ fl. oz.

Weekly.

Tobacco (Sundays)	2 oz.
or cigarettes No. 41 or sweets	4 oz.
Matches (boxes)	2

The Indian ration now contained as protection against scurvy :—

Potatoes or fresh vegetables, such as onions	6 oz.
Fresh fruit	2 oz.
Fresh meat	6 oz.
Tamarind or Cocum	2 oz.
Lime juice (three times a week)	½ oz.

This ration proved satisfactory, but the great difficulty up to March 1917 was its conveyance to the troops.

During the latter part of 1916, owing to the high incidence of scurvy amongst the Indian troops, it was ordered that when there was a shortage of vegetables and fruit they should have the first call on the issues available.

Towards the end of 1916 the transport was much improved and the refrigerator barges which arrived with cold storage chambers for fresh meat were of great value. Also special crates were devised for the conveyance of fresh vegetables and fruit up river, so that as little damage as possible occurred in transit.

After the occupation of Baghdad, local supplies of fresh vegetables and fruit and meat were obtainable in abundance for troops in the front area, and from this time scurvy almost disappeared from the force. The few cases that afterwards occurred were amongst Indian troops in distant places in the desert where there was, for some special reason, difficulty of transport of vegetables and fruit.

Baghdad and the area around it was a fertile source of supply of vegetables and fruit of fine quality, which were grown in abundance in irrigated areas by the native population. The following fruit and vegetables were obtainable :—

Vegetables.

A.—Summer planting commencing from the month of February.

Onions.
French beans.
Haricot beans.
Brinjals.
Lady's finger.
Tomatoes.
Cucumber.
Pumpkin.
Melons.
Water melons.

B.—Winter planting commencing from the month of September.

Cabbage.
Beans.
Spinach.
Beetroot.
Carrots.
Turnips.
Radish.
Cauliflower.
Lettuce.
Purslane.

Fresh Fruits.

A.—Fruit produced during the summer locally.

Apricots.
Apples.
Peaches.
Plums.
Grapes.
Figs.
Dates.
Pears.
Mulberries.

B.—Fruit produced during the winter locally.

Oranges.
Tangerine oranges.
Sour oranges.
Lemons.
Limes.
Quince.
Pomegranates.
Citron.

It will be seen that many of them are rich in antiscorbutic vitamine.

A difficulty with which the military authorities had to contend in protecting troops from scurvy was the danger of intestinal infection from the eating of raw vegetables or fruit. This was particularly the case in Mesopotamia where dysentery, enteric group disease and cholera always had to be reckoned with. Orders were issued that vegetables or fruits with an outer skin or rind should be washed in chlorinated water before consumption, but green vegetables, such as lettuce, were to be cooked rapidly, as the risk of infection from imperfect washing was so great.

The Mesopotamia campaign gave additional proof that fresh meat has important antiscorbutic value. During 1916, when the troops at the front, both British and Indian, were unable to get fresh vegetables or fruit for long periods, the only protection that the British had over the Indians was the fresh meat allowance of 1 lb. daily. Usually two or three issues were obtained from local supplies of Arab sheep; on other days tinned beef was issued. The Indian troops usually had only one or two rations of 6 oz. a week. On other days, owing to their caste prejudices, tinned meat could not be issued.

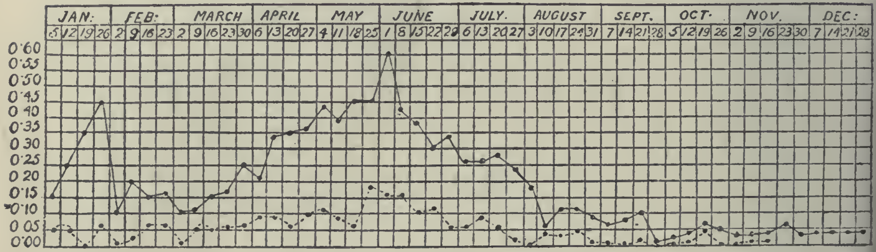

Chart I.—Showing admission rate to hospital per mille of Indian strength. Upper curve = 1917. Lower curve = 1918.

Further evidence of the value of fresh meat was obtained by investigations carried out by Major Marjoribanks, I.M.S., on Indian patients suffering from scurvy, in 1916, at Nos. 9 and 10 Indian General Hospitals. Two parallel groups of scurvy were treated on identical lines as regards diet, except that one group was given a daily ration of fresh meat juice, with the result that they improved much more rapidly than the other patients.

The climatic condition of Mesopotamia and the risk of parasitic infection prohibited the general use of raw meat juice in the treatment and prophylaxis of scurvy, but in the treatment of cases of scurvy in hospital the beneficial effect of a liberal allowance of fresh meat was very striking.

The ration lime juice up to the end of 1916 had no antiscorbutic value, and produced no beneficial effect on patients suffering from scurvy. It usually arrived in Mesopotamia after a long journey overseas, and was probably six months or more old before issue. In August 1916, on Colonel Willcox's suggestion, fresh lime juice was prepared in India from fresh limes, a small quantity of alcohol (5 per cent.) and salicylic acid (2 grains to the pint) being added as a preservative. This was sent to Mesopotamia in special casks, with the date of preparation marked on it, and gave better results as regards antiscorbutic properties; it was used in the treatment of patients suffering from scurvy as well as for issue to troops.

Lime juice as a prophylactic against scurvy is of uncertain value, since it is difficult to ensure its delivery to an army in the field within three months of its preparation, and after that time much of its antiscorbutic value is lost. Undoubtedly when fresh it has important antiscorbutic properties, as was demonstrated on many occasions in patients suffering from scurvy. After the occupation of Baghdad, lime juice was prepared from limes and bitter oranges obtained locally; preservative was added as above described. It was issued to the troops with as little delay as possible. Lemon juice is, however, of superior value to lime juice as an antiscorbutic, according to the recent investigations by Miss Chick and Miss Hume.

In a paper of historical interest by Miss Alice Henderson Smith it is stated that "lime juice" was introduced as a ration for the British Navy in 1804, but that up to 1875 lemon juice was in fact issued under this name. Since 1875 the "lime juice" supplied has been the true lime juice from the West Indies, and would therefore be much inferior in antiscorbutic value to lemon juice. On this point control experiments were made on selected cases of scurvy in Northern Russia in 1919, by Captain A. J. Stevenson, who found that the addition of 4 oz. of lemon juice freshly prepared from fresh lemons gave markedly beneficial results.

The antiscorbutic value of the Indian dried fruits, tamarind, cocum and mango has recently been experimentally investigated by Chick, Hume and Skelton. From the results of their experiments on guinea pigs it was found that all of these had a definite but small antiscorbutic value, greatly inferior to raw cabbage, swedes, germinated pulses, orange or lemon juice, but equal or superior to that of carrot, beetroot, cooked potato, or raw meat juice. Tamarind was taken by the Indian troops either as a chutney with stewed meat, or as an infusion with sugar, when it formed a palatable acid drink. Cocum is a sort of dried plum, which appeared to have no antiscorbutic value on man.

The discovery of the value of germinated lentils (dhall) as an antiscorbutic gives to forces in the field, where no fresh vegetables or fruit are available, a very valuable antiscorbutic prophylactic. Unfortunately, during the trying periods of 1915 and 1916 in Mesopotamia, when antiscorbutics were not available for the troops at the front, this was not known. After May 1917 germinated dhall was used in outlying districts in Mesopotamia as a ration when fresh vegetables or fruit could not be supplied. It was used also in hospitals for the treatment of scurvy, but it had no advantage over the use of fresh fruit and vegetables, and was less palatable. The great value of germinated dhall is that it can be used as a good substitute for fresh fruit and vegetables when these are not available; it is not meant to take their place. Peas or lentils should be neither milled nor decorticated. They should be steeped in water at 50° or 60° F. for twenty-four hours, or at 90° F. for twelve hours. The water should then be drawn off and the seed should be left in the air, but kept moist by covering with wet sacking for twenty-four to forty-eight hours, when they will have visibly begun to sprout. An important precaution in the use of germinated lentils is the avoidance of over-cooking; the period of cooking should not exceed thirty minutes.*

In Northern Russia, Captain A. J. Stevenson, in a series of controlled experiments on scurvy cases, showed very good results with an addition to the dietary of 8 oz. daily of germinated peas cooked for half an hour; the improvement corresponded to that obtained with 4 oz. of fresh lemon juice. Germinated beans gave slightly inferior results. Germinated peas and beans formed part of the ration of the British troops in Northern Russia in the winter season 1918–1919, when fresh foods were unobtainable, and this no doubt explains their immunity from scurvy during that period.

Fresh milk is known to have poor antiscorbutic properties. In Northern Russia, Captain Stevenson tested the effect of milk fermented with lactic acid organisms, two pints daily being given as an addition to the dietary in a series of controlled dietetic tests on scurvy cases. The results obtained were good and corresponded to those yielded in similar groups of cases by 4 oz. of lemon juice and 8 oz. of germinated peas.

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* An interesting historical fact in connection with the use of germinating peas in the treatment of scurvy has been recorded in a "Retrospective view of Naval Medical Conditions," by Sir Robert Hill, the Director-General of Medical Services in the Admiralty, read at the War Section of the Royal Society of Medicine, on 10th November, 1919. He states that "In 1807, in a ship serving on the East Indies Station, the surgeon gave his scorbutic patients 'green peas soaked in water and allowed to vegetate,' with excellent results, a method which is interesting in view of recent pronouncements on the subject of scurvy, and shows how often throughout the ages an old remedy comes to the fore again in its turn."

It remains to be proved whether lactic acid milk is actually rich in vitamine or acts indirectly by preventing harmful intestinal bacterial fermentation.

With regard to climate as affecting the incidence of scurvy, the maximum incidence in Mesopotamia was in the hot months May, June and July, and this appeared to be due chiefly to the difficulty of getting fresh vegetables at that season. In Northern Russia scurvy commonly occurs in the late winter months owing to the difficulty of obtaining fresh foods during the cold season.

Mental depression, fatigue, conditions involving hardship and intercurrent diseases act as predisposing causes. Patients suffering from such diseases as dysentery, those of the enteric group, and epidemic jaundice, which required careful dieting, rapidly developed scurvy unless care was taken that antiscorbutics formed a part of the dietary. It was remarkable how quickly scorbutic symptoms would develop in Mesopotamia in such patients on a dietary devoid of antiscorbutics; patients were seen to develop typical scorbutic gums within six weeks of admission to hospital. It became a rule, therefore, to add to the diet of all patients in hospital a sufficiency of antiscorbutics such as lemons, limes and oranges.

The influence of race shows itself indirectly in dietetic peculiarities. Thus in Indians—where the individual is commonly quite satisfied with a diet consisting mainly of flour or rice, with sugar and condiments, does not complain if only a limited allowance of fresh vegetables or fruit is given him, and commonly dislikes meat—there is a racial predisposition to scurvy. But race has no influence if the dietary is adequate as regards vitamine content.

The knowledge of scurvy has been placed on a sure foundation by the experimental work on animals during the last few years.*

By means of experimental dieting the vitamine content of a large number of foodstuffs has been carefully tested on guinea pigs and other animals and their approximate value determined.

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* Much of this work has been done at the Lister Institute in London, and an important paper was read at the Society of Tropical Medicine and Hygiene, 16th February, 1917, by Miss H. Chick and Miss M. Hume.

Lieut.-Colonel R. McCarrison, I.M.S., has shown, from a number of animal experiments, the wide-reaching effects of a vitamine deficiency diet. Changes occur in many of the most important organs of the body and disordered endocrine function results. Thus a scurvy-producing diet caused in guinea pigs an enlargement of the suprarenal glands due to hæmorrhagic infiltration and cellular disintegration of the cortex and medulla.

Morbid Anatomy.

Externally in white-skinned subjects purpuric rashes and skin hæmorrhages are usually present and also œdema. Characteristic changes in the gums are usually present. Hæmorrhages occur in the muscles and tissues generally, and are commonly seen on the serous membranes of the internal organs. Sanguineous effusions are common in the pleura, peritoneal cavity, and joints, and under the periosteum of the bones. These consist of altered blood which may have undergone partial clotting or even organization into fibrous tissue. The heart muscle shows degenerative changes, brown atrophy often occurring. Degenerative changes occur in the liver, kidneys and other organs. It is probable that in human scurvy, hæmorrhagic swelling and degeneration of the suprarenal glands, and a general thinning and atrophy of the whole intestinal tract occur, such as has been found in experimental work on monkeys by McCarrison. These signs do not appear yet to have been specially described.

Symptoms.

With regard to the incubation period, while it is not possible to give any definite period, it is known that the deficiency in the diet may exist for from four to eight months before symptoms appear.

The symptoms in individual cases vary much in severity and may conveniently be classified into three groups.

Group 1.—Mild, show slight gum changes, anæmia, debility, and possibly skin hæmorrhages.

Group 2.—Of moderate severity, show marked gum changes, hæmorrhages into skin, palate, and possibly into muscles. Anæmia and debility are more marked.

Group 3.—Severe, show marked gum changes and hæmorrhages into palate, skin, muscles, joints or periosteum; the constitutional symptoms, anæmia, debility and cardiac weakness, are severe.

Early symptoms are anæmia, weakness, sore and bleeding gums, pains in the legs, and in white races skin rashes of a purpuric type. It is important to remember that while skin changes such as purpuric rashes, earthy colour, and discoloration are very common in white races, in Indians and dark-skinned races these signs cannot usually be detected.

Dr. H. Wiltshire has called attention to hyperkeratosis of the hair follicles as a very early sign. This sign, however, may occur in other diseases associated with malnutrition.

A hyperplastic condition of the gums with a tendency to hæmorrhage on pressure is a very common early sign. The gum tends to project in the spaces between the teeth, forming characteristic red buds ; this change is often seen best on the buccal aspect. Later, marked swelling of the gums occurs owing to hæmorrhagic exudation, and the appearance may be that of a fungating hæmorrhagic swelling, resembling a new growth. As was seen in many of the Mesopotamian cases, ulceration and sepsis may occur at this stage, the condition of the mouth being very offensive. Gum changes occur in about 90 per cent. of cases, but they may be absent even in severe cases. Captain Sheppard observed in some of the very early cases of scurvy that the gums often showed a rolled edge, running across which fine parallel clawlike striations might be seen, and he was of opinion that this sign was never due to pyorrhœa.

Pyorrhœa is often present and is likely to result as a secondary condition of the scorbutic changes.

Palate changes are of frequent occurrence and are of important diagnostic value, especially in Indians. The palate is pale, and small petechial hæmorrhages, or sometimes patches of a larger size are seen on the hard or soft palate or on the pillars of the fauces. Dark crimson or purplish patches of discoloration are commonly seen extending upwards from the gums of the molar teeth on the inner aspect of the mouth. The petechial patches may become brown when old. It is important, however, in Indians to distinguish hæmorrhagic pigmentation from the natural pigmentation which may be present on the mucous membrane of the mouth or tongue.

The skin is dry, rough, and may be pigmented or of an earthy colour in white races. Small petechial hæmorrhages are very common in white races round the hair follicles of the legs and may occur in other parts of the body. They were observed in some Indian cases, but were difficult to detect. Other scattered petechiæ may occur on the skin. Subcutaneous hæmorrhages occur as irregular purplish patches, especially in exposed parts, and undergo the usual changes in colour. They are not apparent in Indians.

Muscle hæmorrhages frequently occur in the calf and thigh muscles, and form a hard, brawny swelling, hot to the touch and tender on pressure. The swelling usually occurs in the calf, round the popliteal space or in the anterior tibial region. Any of the muscles of the body may, however, be affected, but hæmorrhages usually occur in the groups of muscles most used, such as the leg muscles in infantrymen and the adductors of the thighs in cavalrymen.

Scorbutic œdema sometimes occurs in the legs or feet and around the tendo Achillis. It is of a firm, brawny type, quite different from cardiac or renal dropsy. It can best be detected around the ankles by viewing the patient from behind, when he is standing. Œdema of a cardiac type may, of course, occur in scurvy when there is marked secondary cardiac weakness.

Joint swellings due to hæmorrhagic effusion sometimes occur. In North Russia contractures were common. They were due to involvement of the muscles round the joint.

Subperiosteal hæmorrhages may occur as hard, tender swellings, usually on the tibia or ulna.

Subconjunctival hæmorrhages, hæmorrhage from the bowel, hæmorrhagic pleural effusion and hæmorrhagic peritoneal effusion occasionally occur.

The blood shows the features of a secondary anæmia. An average count of 50 cases reported by Captain Stevenson from North Russia was :—

Red cells	4,080,000	Large lymphocytes ..	20%
Hæmoglobin	55%	Small lymphocytes ..	29%
Colour index	0·68	Eosinophiles	4%
White cells	7,510	Mononuclears	2%
Polymorphonuclears ..	45%		

Coagulation time did not appear to be much affected ; 10 cases in North Russia gave an average of 3·5 minutes.

Alkalinity was tested in a few cases in Mesopotamia, and a few in North Russia. The alkalinity was somewhat diminished, but the observations made were not sufficient to draw definite conclusions as to the extent of the diminution.

Dyspnœa on exertion is often present, and sometimes giddiness. The severe cases show cardiac dilatation with rapid pulse and usually systolic murmurs.

Hæmaturia was observed in 4 per cent. of a series of 50 cases in North Russia and albuminuria in 6 per cent.

Night blindness occurred in 7·4 per cent. of a series of 200 marked cases in North Russia. This symptom was present in the indefinite cases of scurvy referred to above as occurring in No. 24 Field Ambulance in France, in August 1915.

Healing of sores on the skin is retarded and ulcers of an indolent nature sometimes occur.

The progress in severe cases is slow even when under special treatment. A few cases may show pyrexia, due, no doubt, to intercurrent sepsis. Occasionally the muscle hæmorrhages suppurate and require surgical treatment. Diarrhœa is a not uncommon complication. Septic pneumonia is an occasional complication of the very severe cases. The mortality in scurvy was low, being only 0·21 per cent in 11,440 cases in Mesopotamia in 1916.*

Prognosis.

Mild cases will completely recover, after appropriate treatment, in a few weeks.

Cases of moderate severity will recover after appropriate treatment, but a period of a few months is required before the patient is fit for active military duty.

Severe cases require a long period of treatment before restoration to a fair degree of health occurs. In young patients several months will be required before they are fit for military duty. In men over 35 recovery to a moderate degree of health should occur, but these patients are not likely to become fit for active military duty, and permanent invaliding from the army is indicated.

Diagnosis.

Diagnosis should usually present no difficulty, but it should be remembered that gum changes are not always present in scurvy. Pyorrhœa is one of the commonest errors in diagnosis, and is a very common disease in soldiers. It can be distinguished from scurvy by the retraction of the gums from the interspaces between the teeth, whereas in scurvy the gum enlarges and extends in the form of red buds between the teeth. Purpura, due to other causes such as rheumatism, drugs, various infections and blood diseases, must be carefully distinguished. Anæmia with cardiac dilatation and purpura, such as is sometimes seen in malaria, is distinguished by the temperature record, enlargement of the spleen and liver, and blood manifestations characteristic of malaria. Famine œdema must also be distinguished.†

Several instances of malingering occurred in Mesopotamia. Thus, artificial œdema of the leg was induced by the tying of a string or puttee round the limb near the knee, the mark of the ligature being obvious. Swelling around joints was artificially produced by the insertion beneath the skin around the knee of a thread which had been soaked in some irritant. Corrosion of the gums, which had been caused by the application of cresol or other corrosive fluid, was seen and readily distinguished from scurvy by the white slough over the affected area and the presence of a similar mark on the opposed mucous membrane of the mouth.

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* The symptoms of and mortality from scurvy observed amongst some thousands of cases in Port Arthur after its capitulation in January, 1905, are of interest in connection with the symptoms recorded in Mesopotamia. (See Report No. 15 of the Medical and Sanitary Reports of the Russo-Japanese War.)

† See Chapter xx.

Treatment.

Treatment should be directed on the following lines :—

1. Rest in bed in the moderate and severe cases, and an ample supply of fresh air with cheerful surroundings.
2. Special dieting, giving a maximum amount of foods rich in vitamine so far as is consistent with the patient's digestion.
3. Local treatment of the mouth, or other parts affected if necessary.
4. General treatment to improve the blood condition.
5. Treatment to improve the mental state, such as occupation and mild exercise in the open air, when the patient's condition admits of this.

The course of treatment adopted in the Special Scurvy Hospital for Indian patients at Baghdad was as follows :—

Rest in bed was essential as long as the anæmia or cardiac dilatation persisted ; also the presence of muscle hæmorrhage, œdema, periosteal or joint hæmorrhages, or other severe hæmorrhagic symptoms, demanded complete rest in bed. A solution of ½ per cent. salicylic acid in alcohol was applied to the gums twice daily. A mouth-wash of alum and carbolic acid was used frequently ; also dental treatment, such as scraping the teeth to remove tartar and extraction of carious teeth, was carried out. A mixture of iron and arsenic in addition to the other measures was administered when anæmia was present.

The diet table was :—

6 a.m.	Tea and biscuits and 2 oz. fruit.
8 a.m.	½ oz. fresh lime or orange juice.
10.30 a.m.	Chappatie or rice with 8 oz. vegetables and two pints fresh milk.
12 noon.	½ oz. fresh lime juice.
2 p.m.	10 oz. fresh fruit.
7 p.m.	Meat 14 oz., vegetables 8 oz.

Tomatoes, cucumbers and onions were given raw ; other vegetables were boiled for twenty minutes.

One of the most effectual remedies for scurvy is a salad made by cutting raw potatoes into very fine slices, and adding slices of onion and a little vinegar.*

Physical exercises were given for twenty minutes twice a day to those patients who were sufficiently well.

In a few isolated cases the muscle hæmorrhages suppurated and required surgical treatment such as incision. The cases of scorbutic hæmothorax required treatment by aspiration.

In North Russia treatment on the above lines was carried out, the diet being accommodated as far as possible to the national habits of the patients. Reference has been made to the excellent results given on a series of eight cases by the daily addition of two pints of lactic acid milk to the dietary. The percentage increase of weight exceeded that obtained by the use of the other special antiscorbutics, such as lemon juice, germinated peas, germinated beans and fresh meat.

With regard to preventive measures, a suitable selection of the items in the ration scale, so that the dietary contains an ample supply of the accessory food factor or vitamine, is the essential measure of prophylaxis. Due precautions must be taken that the food is not over-cooked.

An important measure where scurvy is occurring in epidemic form is the establishment of special hospitals for treatment of cases, with a special medical officer in charge. By the maintenance of a register of all the cases and a record of all details in each case, the occurrence of scurvy in any unit is at once recognized, and special preventive measures can be adopted without delay. Also accuracy of diagnosis and suitable special treatment are ensured. In Mesopotamia the Director of Medical Services established this procedure in Baghdad, Basrah and Amara, in June 1917, and its adoption gave most satisfactory results.

A convalescent camp for cases of early scurvy was established in the 7th Divisional area on the Mesopotamian front in October 1916. Captain A. L. Sheppard, I.M.S., was in command of this, and notes by him on the early diagnosis of scurvy were circulated throughout the division by the Assistant Director of Medical Services. The object of the scurvy camp was to provide cases of early scurvy with a suitable dietary which would enable them to return to duty at the shortest period. In the very early cases success was achieved, but cases showing marked scorbutic symptoms, such as œdema or muscle hæmorrhages, were found to improve so slowly as to need evacuation.

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* At Colonel Willcox's suggestion this was tested in 1916 on cases in the scurvy camp at the front area by Captain A. L. Sheppard, I.M.S. He found that it gave a better result than any of the antiscorbutics he was then using.

Since the rationing of troops or of a civil population is carried out usually by men who do not possess special medical knowledge, education in the scientific principles which form the basis of a sound dietary is of the utmost importance. For this purpose official memoranda on scurvy and beri-beri were circulated in Mesopotamia, not only to all the medical units, but to the commanding officers of all combatant units in the force. This education of the fighting forces in the principles of rationing as regards protection from the deficiency diseases proved of great value.

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CHAPTER XIX.

BERI-BERI.

BERI-BERI is defined as a disease primarily due to the deficiency of a certain accessory food factor or vitamine in the food consumed over a long period, and characterized by multiple neuritis, œdema, cardiac weakness and muscular atrophy.*

No large outbreak of beri-beri occurred during the war, due no doubt to the preventive measures adopted in the light of recent knowledge of its causation. The disease has long been recognized as endemic in Japan, China, the Malay Peninsula and the East Indies, including the Philippine Islands, Java and the Dutch Indies. The Persian Gulf has been well known as an endemic centre from the frequent occurrence of cases amongst men long stationed there. Isolated epidemics have occurred in England, Ireland, America and various parts of the world.

During the war, limited outbreaks of beri-beri occurred in men from all parts of the world where the disease is endemic, in Chinese labour corps, in Indian labour corps and in Chinese sailors. In the last three months of 1915 a few cases of beri-beri occurred amongst British troops at Gallipoli and at Mudros. The primary cause was considered to be vitamine deficiency, and predisposing causes were the conditions of hardship inseparable from the campaign, and in many of the cases the influence of intercurrent disease. No general outbreak of beri-beri occurred, however, and individual variations in dietary due to some accidental cause could be traced in many of the cases. The campaign was not of sufficiently long duration to put the rations to a severe test as regards their vitamine sufficiency.

Beri-beri cases also occurred in Mesopotamia in British troops. Indian troops were practically free from the disease, the reason of which will be explained in considering the ration scales for the force. The admissions and deaths from this disease amongst British troops in Mesopotamia were :—

		Admissions.	Deaths.
6th November, 1914, to 28th February,	1916	325	Not recorded.
1st July to 31st December ..	1916	104	3
	1917	84	0
	1918	51	6

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* The word " beri-beri " is said to be derived from a Cingalese term meaning " I cannot," expressive of the marked muscular weakness usually present.

The figures given up to 28th February, 1916, are those obtained from hospital records, but as accurate statistics are not available during this period, it is likely that the actual number of cases was considerably in excess of this figure. Records of the number of deaths are not available. The cases occurring during this period were of a severe type.*

The cases occurring after 1st July, 1916, were of a mild type, as is evidenced by the small number of deaths. Also in the British cases, during this period, vitamine deficiency was not the sole ætiological factor.

The occurrence of beri-beri in Mesopotamia in British troops in considerable numbers, up to July 1916, is to be explained by the vitamine deficiency of their rations, as will be described later.

In December 1916 an outbreak of beri-beri occurred in a battalion stationed at Shaiba in Mesopotamia. Sixty cases were reported up to 24th December, 1916, and no deaths occurred. The epidemic was investigated by the consulting physicians to the force, Colonel W. H. Willcox, A.M.S., and Lieut.-Colonel H. G. Melville, I.M.S. Clinically the cases were of a mild type, but the majority, 80 per cent., showed cardiac dilatation, and some symptoms of early multiple neuritis were present in all. The knee jerks were present in 75 per cent. of the cases, and some weakness of the legs was a common early symptom ; a few cases showed anæsthesia. Slight œdema over the shins and ankles occurred in 30 per cent. of the cases, but quickly disappeared with rest in bed. Under appropriate treatment many of the cases improved rapidly and were able to return to duty after a few weeks in hospital. The battalion had been encamped at Shaiba since 15th July, 1916, and the period before development of the early symptoms was between four and five months.

Evidence of vitamine deficiency was found. There was overcooking owing to the hardness of the Shaiba water. The cooking of vegetables was stated by the cook in charge to require five hours, and this was the time allowed for the preparation of the stews for the men. Also, owing to the hardness of the water, lentils could not be cooked, and were in consequence discarded from the ration. The oatmeal supplied to the battalion was badly contaminated with weevils and could not be issued as a ration. Marmite, a form of germinating yeast, the use of which is described below, had only been issued on four occasions, and then had been added to the stews and probably cooked for too long a time. The bread issued to the battalion was made from British flour from which the germ and aleurone layer of the grain were absent.

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* An account was also published in the British Medical Journal, 6th January, 1917, of a medical meeting held at Kut on 1st April, 1916, during the time that troops were besieged and on very short rations, when a clinical demonstration of twenty-six cases was given by Captain E. G. S. Cane, R.A.M.C. These cases were quite typical in their symptoms and were all severe.

In addition to the vitamine deficiency factor, other toxic causes were found amongst many of those affected. 53·5 per cent. of the cases had a history of malaria, of which 20 per cent. had attacks of malaria while in hospital, the parasites being found in their blood. In two cases there was a history of recent jaundice, and a few gave a history of dysentery.

The consulting physicians consequently recommended a supply of Euphrates water for drinking and cooking, the daily issue of marmite, the issue of bread made with flour containing 33⅓ per cent. of atta, an issue of dhall thrice weekly, and the avoidance of undue exertion on the part of the troops, since fatigue appeared to be a predisposing factor in some of the cases. No further cases of beri-beri occurred in the battalion at Shaiba after the adoption of these measures.

The outbreak at Shaiba was also investigated by the War Office Advisory Committee during their visit to Mesopotamia at the end of 1916, and on their advice special bacteriological examinations were carried out by Major W. H. Stevenson.

The cases in the above outbreak were of a much milder type than those which occurred in the Mesopotamian force previous to 1st July, 1916, and in many of them, as stated, some toxic factor such as malaria was an additional ætiological factor.

It is interesting to record that in December 1917 a slight outbreak of similar cases, nine in number, occurred in the same battalion, which had been moved from Shaiba to Nasiriyeh in April 1917. Major W. H. Stevenson, I.M.S., made a careful investigation of these cases and reported that there was no evidence of vitamine deficiency. He considered that these cases were due to some infective cause, and found that dysentery and tonsillitis had been present in this battalion to a much greater extent than in other units in the area. He regarded the cases as toxic multiple neuritis, and not beri-beri.

Amongst Asiatics, beri-beri was almost confined to Chinese. A very severe outbreak occurred amongst the men of a Chinese porter corps from Singapore during the months of April to August 1917. This corps arrived in Basrah in two drafts, the first in January and the second in April. Cases occurred in both drafts while on the voyage, and some were landed in Bombay. Beri-beri became very severe in the beginning of April, and in the succeeding three months over

500 cases were admitted to hospital from the unit. The corps became quite unfit for work, and the small number eventually left had to be repatriated. The Chinese of the porter corps were on a special diet composed as follows :—

Daily Issue.			*Weekly Issue.*	oz.
Rice	28 oz.	*Sunday*	Pickled vegetables	4
Meat	12 ,,		Sardines	3
Vermicelli	4 ,,	*Monday*	Pickled vegetables	4
Cooking oil	2 ,,		Salt pork	3
Salted eggs	½ each.	*Tuesday*	Dried potatoes	3
Salt	⅔ oz.		Dried fish	3
Pepper	$\frac{1}{50}$,,	*Wednesday*	Pickled vegetables	4
Vinegar	$\frac{1}{50}$ pt.		Sardines	3
Sauce	½ oz.	*Thursday*	Pickled vegetables	4
Garlic	2 ,,		Salt fish	3
Ground-nuts	1 ,,	*Friday*	Dried vegetables	3
Chinese green peas	1½ ,,		Sardines	3
Tea	1 ,,	*Saturday*	Pickled vegetables	4
Sugar	½ ,,		Dried fish	3

The rice was "Siam rice," which had been brought from Singapore by the corps. It was husked and polished rice, which in Singapore had been looked upon as a suspicious beri-beri producer. The Chinese preferred a rice of this sort, and considered any other grade of rice containing proportions of husk and pericarp to be an inferior issue. As a result of an enquiry into the outbreak, a new scale of diet was drawn up for the Chinese composed as follows :—

Bread (made with 25 per cent. atta)	12 oz.
Rice	12 ,,
Fresh meat	12 ,,
Vegetables	4 ,,
Dhall	4 ,,
Fresh potatoes	4 ,,
Salt fish	3 ,,
Tea	1 ,,
Sugar	2 ,,
Cooking oil	1½ ,,
Marmite	¼ ,,

The rice supplied was the ordinary variety issued to Indian troops. Fresh fish was supplied when available. Beri-beri was well established before the introduction of the new diet, and no immediate successful result was obtained by its use on the porter corps. Very few cases of beri-beri occurred amongst Indians, and of the cases occurring amongst Chinese after the departure of the Chinese porter corps most were in Chinese employed by the Inland Water Transport department. In all, 31 deaths from this cause occurred during the period, giving a case mortality of 5·4 per cent.

The Chinese were, however, very obstinate in their prejudice in favour of polished rice, and the director of medical services brought the facts to notice with a view to disciplinary action in certain cases.

Several cases were observed amongst Chinese sailors on ships arriving at Basrah. The cause was an obvious vitamine deficiency in the dietary. Lieut-Colonel C. A. Sprawson, who was consulting physician at Basrah, made a special investigation into the cases reported as beri-beri during the later period of the campaign. He concluded that the cases occurring on ships in Mesopotamia were entirely due to vitamine deficiency, that the cases occurring amongst the Chinese labour corps in Mesopotamia were due to a vitamine deficiency pre-existing before arrival in the country, and accentuated by fatigue and other predisposing factors, while the British cases occurring in the later stages of the campaign he regarded as due to some infective cause and not to vitamine deficiency.

In some of the Indian labour corps attached to the 3rd Army in France, an outbreak of beri-beri was recorded in January 1918. The epidemic was investigated by the A.D.M.S. Sanitation, France, and the cases, though typical of the disease as regards their symptoms, were of a mild type. The outbreak was due to the main portion of the ration being of polished rice, the unpolished variety, though ordered, having been unobtainable. The vitamine deficiency was remedied by the substitution of 1 lb. of atta for 1 lb. of the 2 lbs. allowed of rice, and an addition of 1 oz. of dhall to the daily ration.

In May 1917, a number of cases were reported at Noyelles amongst Chinese labourers who had recently arrived in France. An investigation showed that the disease had developed during the voyage, and was undoubtedly due to a vitamine deficiency in the rations received on board ship, polished rice having been given during this period.

The cases were quite typical as regards their clinical symptoms, and quickly improved under suitable dietary in hospital. On arrival in France the rations for the Chinese labour corps were carefully adjusted as regards vitamine content and further cases of beri-beri did not occur amongst them.

Twenty-four cases reported as beri-beri were transferred from Indian transports on arrival at Marseilles on 25th September, 1914. Nineteen of the cases were from two British battalions, which were stationed at the same cantonment in India and had encamped together on mobilization, and later travelled to Europe on the same transport. The remaining five cases were from another British battalion. They arrived at Marseilles after a long voyage broken by a short stay in Egypt. The men stated that they had suffered from the heat on the voyage, that the troop decks were very crowded, and that at night the air was stifling. The food had been good throughout, with the exception of the bread, which was described as doughy. The ætiology of these cases as regards vitamine deficiency appeared obscure, and they were probably cases of multiple neuritis of toxic origin.

During the war cases of beri-beri were reported from time to time at various ports amongst Chinese and Lascar sailors. These were due to a vitamine deficiency of the ship rations, polished rice usually being the offending article in the dietary.

In the campaign in German East Africa, some cases of apparently typical wet beri-beri and instances of peripheral neuritis were found in the hospital carrier "Morogoro" and in other carrier units. The Seychelles porters repatriated from Kilwa early in 1917 developed a severe form of the disease between Kilindini and Port Louis, and they appear to have exhibited symptoms of it when proceeding by sea from Kilindini.

Ætiology.

It has been conclusively proved that the essential cause of beri-beri is the continued absence, over a long period, of an accessory food substance or vitamine in the food consumed. It has at various times been supposed that the disease was primarily due to chemical poisoning, such as chronic arsenical poisoning, chronic oxalic acid poisoning, or poisoning from toxic products in certain types of food such as fish and rice; to deficiency of protein, fat, combined phosphorus, or cholesterin in the dietary; or to infective causes such as some animal parasite of the protozoal group, some worm such as *Ankylostomum duodenale*, or to some vegetable parasite such as a specific coccus, bacillus or fungus. These theories must in the light of recent knowledge be abandoned.

Infective causes, however, in the absence of vitamine deficiency, while not causing beri-beri, may give rise to an illness associated with multiple neuritis, cardiac weakness and dropsy, and the clinical picture is then indistinguishable from beri-beri. Cases of this type should be regarded as multiple neuritis due to the particular infection concerned. Where there is deficiency in the dietary of vitamine and an infective element is superadded, for example, jaundice, diarrhœa or malaria, the latter acts as a strong predisposing cause to an illness presenting all the characters of beri-beri. Examples of this were seen in some of the Dardanelles cases and also in some of the cases in the Shaiba epidemic in Mesopotamia.

Outbreaks of beri-beri have undoubtedly varied as regards their ætiological factors. Thus those due to a dietary consisting mainly of polished rice may have as the sole cause vitamine deficiency, while other outbreaks have been described where, in addition to a vitamine deficiency, some other toxic influence was at work.

The beri-beri preventive vitamine appears to be identical with the " water soluble B " factor first described by McCollum and Davis. A large number of attempts have been made to obtain this accessory food factor in a pure condition, but success has not been yet achieved.

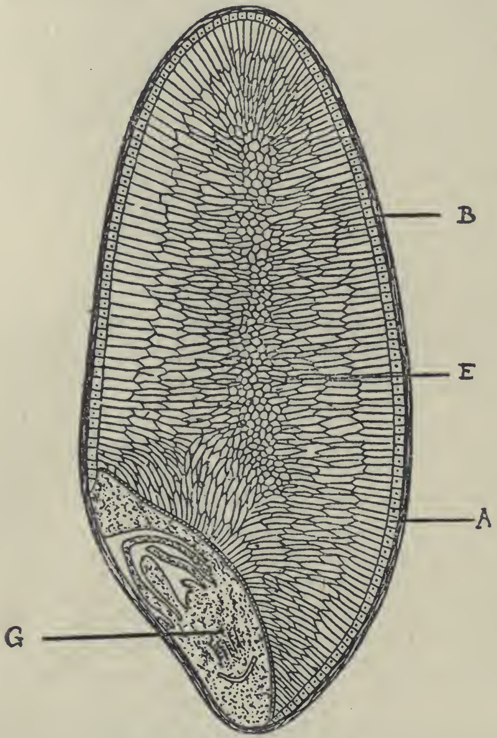

Fig. 1.—Diagram of a longitudinal section through a grain of wheat, showing : *B*—Pericarp, forming the branny envelope. *A*—Aleurone layer of cells forming the outer-most layer of the endosperm removed with the pericarp during milling. *E*—Parenchymatous cells of the endosperm. *G*—Embryo or germ.

This vitamine is much more stable than the anti-scorbutic vitamine. The former withstands desiccation for long periods of time, and its resistance to heat is considerable; the contrast being very marked in these respects. Thus, heating for two hours at 100° C. causes only slight loss of the anti-beri-beri vitamine, but temperatures much above 100° C., such as those approaching 120° C., result in a rapid destruction.

The baking of bread or biscuit, during which process the interior of the material does not rise above 100° C., therefore causes no serious diminution in anti-beri-beri vitamine. On the other hand, the canning of food stuffs involves frequently a much higher temperature than 100°, so that tinned foods of all descriptions may usually be regarded as vitamine-free.

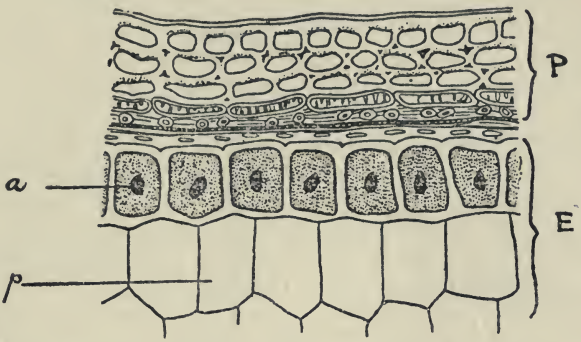

Fig. 1A.—Cross-section through the branny envelope and outer portion of the endosperm of wheat grain, showing: *P*—the pericarp; *E*—endosperm, consisting of *a*, layer of aleurone cells and *p*, parenchymatous cells.

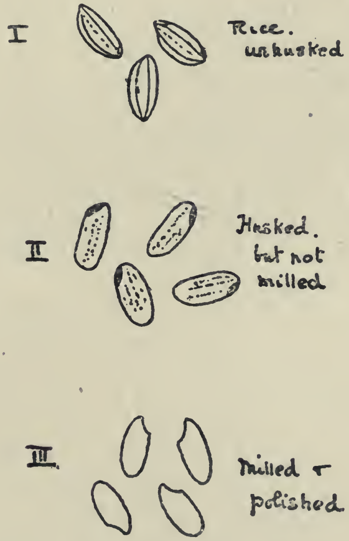

Fig. 2—Showing the various stages in milling of the rice grain. I.—Rice grain in the natural condition, retaining the husk or enclosing glumes. II.—After removal of the husk, but retaining the pericarp or "silver-skin," and the embryo, which is shaded. III.—After milling and polishing; both "silver-skin" and embryo are removed, and the grains are then "polished" by rubbing with talc between sheepskins.

The anti-beri-beri accessory factor is fairly widespread amongst natural foodstuffs, and during recent years much experimental work has been done by Cooper, Chick, Hume and others, in order to determine the approximate quantitative distribution of the protective factor. It is found chiefly in plant seeds and in the eggs of birds. The most important source, from the practical point of view of drawing up scales of rations, is cereals. It has been found that the vitamine is differently distributed in different parts of the grain or seed. The largest proportion exists in the embryo or germ, and next in order is the bran (pericarp and aleurone layer), while the endosperm, or starch-containing portion (for example white wheaten flour or polished rice), is greatly deficient in the vitamine. There is no doubt that this differentiation holds amongst all cereals, though the experimental work has dealt mainly with rice and wheat. It is illustrated in the accompanying diagrams (Figs. 1, 1A and 2).

Yeast, eggs, the various pulses, such as peas, beans and lentils, are rich in the vitamine. Heart muscle, liver, brain and kidneys contain a fair proportion, while milk and the muscle-fibre of meat are comparatively deficient.

The history of beri-beri in the Mesopotamian expeditionary force up to 1st July, 1916, furnishes an excellent example of its causation by the absence of the essential vitamine in the dietary. The Indian troops received throughout the campaign a daily ration of atta* 1½ lb., and dhall 4 oz., both of which are rich in anti-beri-beri vitamine. In spite of the hardships to which they were subjected they remained free from beri-beri. The British troops, from the commencement of the campaign on 6th November, 1914, up to 4th July, 1916, received rations according to the scale of field service rations given in War Establishments, India, 1916.†

The bread or its substitute, biscuits, issued to British troops during this period was made from white flour from which the wheat germ and pericarp and aleurone layer had been removed ; it therefore contained practically no anti-beri-beri vitamine. The small amount of the protective factor present in fresh meat and potatoes would probably be sufficient to prevent the occurrence of beri-beri. But owing to the exigencies of the campaign up to 1916, fresh meat and potatoes were often unobtainable for long periods, and the main articles of the dietary of the British soldier in the front area were then tinned meat and biscuits, both of which lack the necessary vitamine. The British soldier thus became liable to beri-beri, and a number of severe cases occurred.

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* A wheat flour prepared in India, containing the germ and aleurone layer of the grain, part of the bran or pericarp having been removed.

† See Chapter xviii, p. 415.

The defect of the British ration as regards protection against beri-beri was fully realized by the medical authorities in Mesopotamia in 1916, and on the representation of the director of medical services the following scale of rations was introduced on 4th July, 1916 :—

Bread	1 lb.	Rice	3 oz.
Fresh meat	¾ ,,	Jam	3 ,,
Bacon	3 oz.	Condensed milk	2 ,,
Potatoes	1 lb.	Salt	½ ,,
Tea	1 oz.	Pepper	1/36 ,,
Sugar	2½ ,,	Oatmeal	4 oz.
Cheese	3 ,,	Condensed milk	2 ,,
		Extras.	
Chocolate	1 oz.	Dates	4 oz.
Bread	4 ,,	Fresh fruit	4 ,,
Lime juice	½ fl. oz.	Dry lentils (dhall)	2 ,,
Sugar	½ oz.	Curry powder	⅛ ,,
Rum	4 fl. oz.	Limes (per man)	3

In this scale the oatmeal and dhall both contain the necessary protective factor.

On 31st October, 1916, a further improved ration scale was sanctioned containing the following articles :—

Daily.	
Bread	1 lb.
Or biscuit when bread not available	12 oz.
Fresh meat	1 lb.
Or preserved when fresh not available	12 oz.
Pickles when preserved meat is issued	1 ,,
Bacon	3 ,,
Potatoes or fresh vegetables	12 ,,
Or dried vegetables when fresh not available	3 ,,
Tea	¾ ,,
Cheese (not in summer)	3 ,,
Sugar	3 ,,
Jam or golden syrup	3 ,,
Tinned milk	2 ,,
Salt	½ ,,
Fresh fruit	2 ,,
Or tinned fruit	2 ,,
Or dried fruit when fresh fruit not available	1 ,,
Soup or Oxo (not in summer)	2 ,,

Weekly.	
Pepper	1/5 oz.
Mustard	1/7 ,,
Twice Weekly.	
Marmite (Monday and Thursday—not in summer)	¼ ,,
Thrice Weekly.	
Oatmeal (Monday, Wednesday and Friday)	3 ,,
Tinned milk (Monday, Wednesday, and Friday)	1 ,,
Curry powder (Tuesday, Thursday and Saturday)	⅛ ,,
Rice (Tuesday, Thursday and Saturday)	2 ,,
Butter (Monday, Wednesday and Friday—not in summer)	2 ,,
Lime juice (Tuesday, Thursday and Saturday—not in winter)	½ ,,

In this scale an issue of marmite twice weekly was added as an additional protective against beri-beri.

In February 1916, Colonel Willcox suggested to the Sanitary Committee of the War Office the advisability of an extract of yeast being issued to the troops as a prophylactic against beri-beri. Experiments were then instituted by Colonel Horrocks and carried out by Professor Starling, Dr. S. M. Copeman, and their co-workers. They showed that extract of yeast was a prophylactic against beri-beri, and the preparation known as marmite was issued to British troops in Mesopotamia in October, 1916. Marmite can be mixed with warm water and taken like bovril or be added to a stew after cooking. It was undoubtedly of great value as a prophylactic against beri-beri in Mesopotamia, and it was a valuable remedy in the treatment of cases that occurred. It kept well in Mesopotamia, and no difficulty was experienced in its issue as a ration to troops.

In February 1917, experiments were also carried out at Amara to determine the practicability of issuing to British troops bread made with a certain proportion of atta in the flour. Loaves were made with flour containing 100 per cent., 75 per cent., 50 per cent. and 25 per cent. respectively of atta. The bread was very palatable, but the addition of much atta caused some difficulty in the rising of the dough, so that the bread was somewhat heavy. Bread made with 25 per cent. of atta was quite as palatable, and differed little, except in the slightly brownish colour, from ordinary bread. It was issued to several units at Amara with satisfactory results, and later on a general issue to the army on three days a week was sanctioned by the General Officer Commanding-in-Chief. The issue to British troops of bread rich in anti-beri-beri vitamines was thus an important factor in the reduction of beri-beri among them. After March 1916, very few cases of beri-beri occurred in the Mesopotamian Force, and these were generally of a mild type, and in them some intercurrent disease was usually an important predisposing factor.

Rice has for many years been associated with beri-beri outbreaks. The recent knowledge on the subject has very clearly defined the part it plays. The polished variety is almost devoid of protective vitamine, owing to removal of the pericarp and germ. Unfortunately, Chinese labourers and other labour corps consider that the polished rice from its white colour is of a better quality, and often object when the unpolished variety, which is brown or reddish in colour, is issued to them. Unhusked rice is known as "paddy." If the husk is removed by steaming or treatment with hot water and subsequent rubbing in a mortar or by hand, as is the case with native rice, the pericarp and germ of the grain are not removed, and this variety of rice is fully protective against beri-beri. The rice germ is one of the richest substances in anti-beri-beri vitamine, and the rice polishings removed by the milling process have long been known to have a high protective value.

The following table gives the comparative values of common articles of food as regards protection against beri-beri, arranged in order of their vitamine content :—

Yeast extract (marmite)	Rich.
Rice germ	
Wheat germ, maize germ	
Yeast	
Lentils (dhall, peas, beans, etc.)	
Egg yolk	Moderately rich.
Liver	
Kidney	
Heart muscle	
Sweetbread, fish roe	
Oatmeal	
Wholemeal bread or biscuits	
Meat	Poor.
Fish	
Potatoes, carrots, fresh vegetables	
Fresh milk	
Meat extract	Vitamine absent.
Tinned meats	
Bread or biscuits (made from white milled flour)	
Polished rice	

Burghoul formed part of the army ration of the Turkish soldier. This is dried parboiled wheat, which was used for making bread, or was added to soups and stews. It was a valuable constituent of the ration from its richness in anti-beri-beri vitamine.

The toxines of other diseases which can of themselves cause neuritis and cardiac weakness may undoubtedly play an important part in the causation of beri-beri. In these cases some vitamine deficiency can be found on investigation, and where the deficiency applies to a ration issued to a large number of persons an outbreak of a considerable number of cases is to be expected.

In the Dardanelles cases an intercurrent disease, such as jaundice, diarrhœa, dysentery, or enteric group disease, was present in several of the cases, but in them the special hospital diet given in consequence of the associated disease was almost devoid of anti-beri-beri vitamine and doubtless contributed towards the development of that disease.

In Mesopotamia the cases occurring in British troops from December 1916 to 1918, were of a mild type and malaria was a complicating factor in a considerable proportion, also the effects of heat, diarrhœal disease, sandfly fever and paratyphoid fever were sometimes predisposing factors. In these cases the knee jerk was often retained and the loss of power only slight or moderate in extent, in marked contrast to the Chinese cases which showed complete loss of knee jerk and great loss of power in addition to the other classical symptoms.

In the latter the predominant and sole cause was vitamine deficiency, whereas in the British cases the vitamine deficiency factor, though present, would probably have been insufficient of itself to cause the disease.

In Mesopotamia beri-beri occurred chiefly during the cold months September to January. Race did not appear to be a special predisposing cause, except in so far as racial peculiarities of diet may expose the individual to greater danger. Age did not appear to be a factor. Infantile beri-beri has occurred in the Philippine Islands to a considerable extent amongst breast-fed infants whose mothers were having a diet consisting mainly of polished rice. Both mothers and infants developed beri-beri. The disease has recently been stamped out by the use of an extract of rice polishings in the dietary. Fatigue may play a part as a predisposing cause. Overcrowding and unhealthy surroundings and depressing influences generally may act as predisposing causes.

A considerable amount of experimental work has been carried out in connection with beri-beri. Polyneuritis experimentally produced in pigeons, rats and other animals is probably identical with beri-beri in man. It is also clearly shown that the anti-neuritic factor is identical with the anti-beri-beri vitamine and with the water soluble B factor. In pigeons fed on a vitamine-free diet, the incubation period appears to be from 15 to 25 days.*

Lieut.-Col. R. McCarrison, I.M.S., in an experimental research on animals, has pointed out that though vitamine deficiency is the essential ætiological factor in beri-beri, nevertheless this is rarely so completely the sole agent as in scurvy. This conclusion is in remarkable agreement with the clinical observations on beri-beri in Mesopotamia. He has also shown that in the experimentally-produced polyneuritis in pigeons there is a chronic inanition, a derangement of the function of digestion and assimilation, and a disordered function of the endocrine glands and of all the organs of the body. Thus the remarkable result was obtained that in experimentally produced polyneuritis a considerable enlargement of the suprarenal glands occurred with a corresponding increase in adrenalin content. On the other hand, atrophy and impaired function occurred in the reproductive glands, in the thymus, in the pancreas and in the spleen. He found that deficiency of anti-neuritic vitamine predisposed to bacterial infections, such as septicæmia and tubercle, and also led to functional and degenerative changes in the nervous system.

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* See Report No. 38 of the Medical Research Committee, 1919, for a detailed account of the experimental work carried out in the past.

Morbid Anatomy.

Post-mortem examinations were made on two of the Dardanelles cases by Lieut.-Col. C. J. Martin. Œdema was present to a marked degree in the lower extremities and to a less extent on the trunk and upper extremities. The heart showed dilatation of the right and left cavities. No valvular disease was present. The heart muscle showed the naked eye changes of fatty degeneration. The lungs were œdematous and congested at the bases. The stomach showed considerable redness of the mucous membrane which was most marked in the pyloric half where the colour was a deep crimson. The duodenum showed intense crimson congestion of the mucosa, especially in the upper part. The jejunum and ileum showed marked congestion, some petechiæ being present in the latter. The large intestine showed congestion. Numerous small hæmorrhagic patches about half an inch in diameter were present in the wall of the ascending colon. The mesenteric glands showed slight enlargement. The kidneys were congested and showed cloudy swelling. The liver was congested and showed slight nutmeg change.

The post-mortem changes in the nervous system have at other times been carefully studied by various observers. No marked changes may be visible to the naked eye, but special staining methods and microscopical examination show extensive degenerative changes in the peripheral nerves, the motor nerves being most affected, the sensory branches suffering to a less degree. Hamilton Wright has shown that the branches of the vagi to the heart show marked degenerative changes, and in acute cases the nerve ganglion cells of the heart and of the first and second pair of the thoracic ganglia show characteristic degenerative changes.

The spinal cord is usually found to be normal. Hamilton Wright and others have described degeneration of the posterior spinal ganglion and anterior cornua of the lumbar cord, together with atrophy of Goll's column, in which histologically there is a thickening of the glia tissue, and a complete disappearance of the nerve fibres with the presence of many granular cells.

The degeneration of the nerve fibres of the peripheral nerves has been carefully studied by Scheube, Hamilton Wright, Baelz, Duerck, and recently by Kimura. The medullary sheath becomes vacuolated, and the axone appears like a wavy cord, or as a series of comma-like segments. Finally, both medullary sheath and axone disappear, while Schwann's sheath collapses and the nerve fibres become lost in the connective tissue of the endoneurium. Along with these changes there is a cellular infiltration of the perineurium and of the endoneurium, and when fully degenerated the nerve may consist simply of connective tissue. In the early stages the degeneration does not always begin in the distal ends of the nerves, but may start at a certain height in a nerve fibre. Also badly degenerated nerve fibres may be seen lying alongside normal fibres. The skeletal muscles may show degenerative changes of a fatty nature or simple atrophy in the muscle fibres, and similar changes have been described in the muscle cells of the heart. McCarrison states, from his experiments in the production of polyneuritis on animals, that paralysis may result from loss of function before actual nerve degeneration has occurred.

Symptoms.

With regard to the period required for the development of beri-beri, Fraser and Stanton found that amongst Japanese fed upon a diet consisting mainly of polished rice, the disease occurred after a period of eighty to ninety days.

Four types of cases are seen.

I. *The Wet or Œdematous Type.*—In this, the commonest type of case, the earliest symptoms are usually some weakness of the legs, or shortness of breath on exertion, generally accompanied by malaise and anorexia. In some cases the swelling of the legs is the first symptom noticed. This swelling is usually marked and the œdema may extend to the thighs, scrotum and abdomen. Œdema over the sternum may occur. It was only seen by Willcox in Chinese cases. Ascites and hydrothorax may occur in advanced cases.

Dyspepsia is a common early symptom, epigastric discomfort and flatulence being complained of. Tenderness on palpation over the duodenum often occurs.

Paræsthesia of the legs occurs early in some cases, the patient complaining of numbness, " pins and needles," or alteration of the tactile sense. The weakness of the legs is shown by inability to march or walk properly, the gait being somewhat unsteady. One of the earliest signs of weakness of the legs is shown by the " squatting test." This test consists in the patient bending his knees and separating them so that he assumes a squatting position with the buttocks a few inches from the ground. A beri-beri patient is then usually unable to raise himself up from this position, and often attempts to do so by climbing up his lower extremities with his hands very much like a patient suffering from pseudo-hypertrophic muscular atrophy. This test should be remembered by regimental officers as a simple way of picking out early cases of peripheral neuritis amongst a body of troops who may be likely to be affected with beri-beri.

Anæsthesia and analgesia are common symptoms and their extent varies much in different cases. In some cases only the feet may be affected and in others the feet and legs. The upper extremities are affected in the more severe cases. There is loss of sensation to a light touch and inability to distinguish between a pin prick and the finger touch over the affected areas. Tenderness of the calves on pressure is often present, and the patients sometimes complain of cramps in the calves. Circumoral anæsthesia occasionally occurs.

The sensory symptoms may be complicated by " functional " anæsthesia. Thus, in one of the Mesopotamia cases a patient suddenly developed complete loss of sensation below the neck. This was of a functional type and cleared up under suggestion as rapidly as it developed.

Motor weakness is shown first in the lower extremities, and is followed by marked wasting in severe cases. The extensor muscles are affected more than the flexors, so that foot and wrist drop occur.

Laryngeal paresis with loss of voice may occur, and also occasionally pharyngeal paresis with difficulty in swallowing, especially liquids.

Gait is affected in severe cases. It becomes unsteady and may be somewhat ataxic in type, with a tendency for the toes to drop, and sometimes a high-stepping gait occurs. The ataxic type of gait has not the stamping character peculiar to tabes dorsalis.

The knee jerks may be increased in the first few days. They are soon, however, diminished and become quite lost even with reinforcement. In some cases observed, the knee jerks disappeared before the Achilles jerk, and when both reflexes were lost the Achilles jerk recovered before the knee jerk.

In cases showing severe multiple neuritis, there may later be contractures of the muscles causing deformities such as talipes. These are, however, rare.

The pulse is usually quickened, especially on exertion. In severe cases it may be feeble and irregular. Palpitation is a common symptom. The cardiac dullness is increased both on the right and left sides. The heart shows signs of myocardial degeneration. The impulse is feeble and the first sound of the heart is short and poor in quality. Often a systolic murmur replaces the first sound of the heart more or less completely. There may be a definite galloping rhythm in severe cases.

Pyrexia is absent in beri-beri cases unless they are complicated by some intercurrent affection.

Vomiting sometimes occurs in the severe cases and is a bad prognostic sign.

Loss of weight is usually marked.

II. *The Dry or Atrophic Type.*—This is similar in its symptoms to the œdematous type just described, except that dropsy is absent. It may be a late stage of the wet type.

III. *The Acute Pernicious Type.*—In this type sudden death may occur without previous complaint of illness, the post-mortem examination showing signs of beri-beri. Usually anorexia, nausea, vomiting and epigastric discomfort occur with marked cardiac weakness. Dropsy is usually present and also some signs of neuritis, such as paresis or paralysis, anæsthesia and analgesia, can be detected. Death usually occurs from cardiac failure within a few days.

IV. *The Mild or Rudimentary Type.*—In this type the symptoms are slight. The patient complains of malaise, dyspepsia with paræsthesia, anæsthesia of the lower extremities and some loss of power. The symptoms rapidly clear up under appropriate treatment. In Mesopotamia, after July 1916, many of the cases were of this type, and were complicated by some intercurrent disease, such as malaria, which was in them an important predisposing factor.

Prognosis.

The prognosis in all except the rudimentary type is grave as regards prolonged invalidism. Complete rest in bed for a long time is usually necessary on account of the cardiac and muscular weakness. Recovery is slow, and a long period, twelve months or more, will generally be required before the patient is likely to be fit for duty. Permanent invaliding from the army is usually indicated in such cases.

In the mild or rudimentary type each case must be judged on its merits. In Mesopotamia many of the cases of this type were able to return to active duty after a few weeks in hospital.

Diagnosis.

The most important and difficult differential diagnosis is that from multiple neuritis due to other causes. It is essential that the utmost care be taken in the diagnosis of beri-beri, since the faulty diagnosis of beri-beri in a case of multiple neuritis from some other cause such as diphtheria may lead to much unnecessary alarm. Such causes of multiple neuritis as diphtheria, enteric fever, malaria, arsenical poisoning, the effects of heat, alcohol, and dysentery were all met with in Mesopotamia, and the cases had to be carefully differentiated from beri-beri, for which they were sometimes at first mistaken. It is important, therefore, that in cases where no vitamine deficiency in diet has occurred, and where there is some obvious cause for the multiple neuritis, the diagnosis of "multiple neuritis" and not beri-beri should be made.

In campaigns where vitamine dietetic deficiencies occur, scurvy and beri-beri may both arise. Errors of diagnosis due to the mistaking of scorbutic œdema of the legs for the œdema of beri-beri must be guarded against. No difficulty should arise since the œdema of scurvy is of a hard brawny type, while that of beri-beri is of the soft type like cardiac or renal dropsy. The other signs of scurvy serve to differentiate further the two diseases.

Diseases of the spinal cord, such as tabes dorsalis, myelitis, and scleroses of various kinds, may be mistaken for beri-beri. A careful examination for such symptoms as lack of bladder control, extensor plantar reflex, and ankleclonus, distinguishes myelitis and sclerotic conditions from beri-beri. In tabes dorsalis, the Argyll Robertson pupil, the marked ataxy, the absence of muscular wasting or tenderness of the calves, are signs distinctive from beri-beri.

Dropsy may arise from other causes such as renal disease, where the presence of albumen and casts in the urine and absence of neuritis are points of distinction, or from cardiac disease, where the history of the case, such as previous rheumatism, syphilis, or other cause of cardiac disease, and the long duration of the symptoms without signs of multiple neuritis make the diagnosis easy.

Epidemic dropsy is distinguished from beri-beri by pyrexia, anæmia and absence of multiple neuritis.

It is important, especially in the case of native troops or labour corps, to remember that ankylostome infection may sometimes closely simulate beri-beri. Symptoms like those of peripheral neuritis are not uncommon in ankylostomiasis, œdema is often seen, and dropsy is a frequent concomitant of severe and advanced cases. The history will usually serve as a guide, but in all cases of doubt the fæces should be carefully searched for hookworm eggs.

Treatment.

With regard to treatment, absolute rest in bed is essential in the early stages of the disease, and until all cardiac symptoms have cleared up.

In an acute case where gastric symptoms are present, the diet will necessarily be light and mainly liquid. A careful selection should be made of suitable articles on the lines laid down above. Thus ¼ oz. marmite should be given thrice daily, or, if that is not available, about 2 oz. daily of yeast, which can be given in a palatable form stirred up with milk and sweetened to taste. The yolks of eggs beaten up in milk, pea soup and oatmeal porridge should form part of the dietary. When solid food can be taken, a careful selection should be made of those articles rich in anti-beri-beri vitamine, which are suitable for the digestive state of the patient.

It is important to remember that the dietary, though mainly directed as curative for beri-beri, must also be protective against scurvy; therefore the juice of two or three fresh lemons or oranges should be given daily.

The after-treatment of the case will be directed on the lines of treatment most suitable for multiple neuritis, such as massage and electrical treatment, care being taken that the diet remains rich in protective vitamine.

The preventive measures depend upon the dietary. A suitable selection of the items in the ration scale, so that the dietary contains an ample supply of the necessary protective food factor or vitamine, is the essential measure of prophylaxis. Early notification of cases is also essential.

As in the case of scurvy, an important measure, where beri-beri is occurring, is the establishment of special hospitals for the treatment of cases, with a special medical officer in charge.*

In Mesopotamia, this procedure was adopted in Baghdad, Basrah and Amara, in June 1917, with most satisfactory results.

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* See Chapter xviii., p. 427.

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CHAPTER XX.

FAMINE DROPSY.

FAMINE dropsy has been described by various writers under the names of hunger œdema, famine œdema; *œdème de la guerre, œdème de la fame; anasarque essentielle; hydrops famelicus; edema da fame; Œdemkrankheit, Kriegsödem, Hungerödem.*

It is described as a form of dropsy associated with bradycardia, polyuria, and asthenia, which occurs in persons subjected to prolonged underfeeding. It is unattended by albuminuria, cardiac dilatation, or neuritis. It affects more particularly men who are called upon to perform hard physical work, whilst their daily food ration contains from 800–1,200 calories. These calories are as a rule embodied in a largely fluid diet which comprises 15 per cent. more of indigestible celluloses with very little fat and a maximum daily allowance of 50 grammes of protein.

The occurrence of dropsy has been recognized as a result of underfeeding and famine since the dawn of literature. Hesiod, in his "Works and Days," speaks of the starvation a hard winter brings, and advises prudent thrift, "lest the helplessness of evil winter overtake thee, and with wasted hand thou press thy swollen foot." Scaliger attributed to Aristotle the remark that in famished persons the upper parts of the body are desiccated, the lower tumified. Hecker, in his account of the destruction of the French army before Naples in 1528, refers to soldiers with pallid visages, swelled legs and bloated bellies, scarcely able to crawl. Sydenham refers to the condition when he makes use of the quotation: "ubi desinit scorbutus, ibi incipit hydrops." He qualifies his quotation by calling it a saying of the vulgar which means that, when a dropsy has shown itself by clear signs, the preconceived notion of a scurvy falls to the ground. Still the connection between scurvy and dropsy in a popular saying suggests that the conditions under which the disease arose were closely allied in the minds of a seventeenth-century public.

Lind, quoting Van der Mye's description of the diseases observed during the siege of Breda in 1625, says: "Of those who were afflicted with the flux few escaped . . . They afterwards became bloated, relaxed and dropsical. Watery swellings of the testicles were frequent . . . Some died early in the disease, viz., those who had seldom any evacuation of blood by the nose or stool and seemed from the beginning indolent, dispirited, and blown up as it were with wind. Their stools were greasy, fœtid, and of various colours, but not frequent." In another passage Lind gives an extract from a letter written by the surgeon of the "America" ship of war, dated 11th November, 1762: "Our long cruise . . . . proved very fatal to our East India squadron; having lost on our return to Madrass eight or nine hundred brave fellows by an extraordinary species of scurvy . . . The disease most commonly began with a soft swelling of the legs, which ascended to the thighs, enlarging them to an enormous size. This swelling afterwards extending itself up to the belly and scrotum gradually mounted up . . . so that . . . the patients laboured under an universal dropsy, accompanied with swelled putrified gums, a stiffness at the joints of the knees, livid stains and scorbutic spots . . . The patient after its first attack seldom survived seven weeks, few lived longer, many expired in a shorter time. They all died of a suffocation from water, except those from whom the water was constantly drained off by means before mentioned; and they after languishing for some time, expired at length when reduced almost to perfect skeletons." In this account scurvy certainly enters, but the dropsy is the novel and most striking feature.

Articles on anasarca, on famine, and on œdema, in the *Dictionnaire encyclopédique des Sciences médicales*, mention famine dropsy as a well-defined entity.

Kollreuther is quoted as the authority for the observation of famine dropsy during Napoleon's retreat from Moscow in 1812; and it is said to have occurred in the Irish famine in 1835.

The first clear distinction between famine dropsy and scurvy, beri-beri, and the various final œdemas of inanition or diarrhœa was made by Cornish. He described the condition with great precision in 1864 as occurring amongst prisoners on certain dietaries in the Madras jails. "Under this system of diet the men became unhealthy and within three months six of the one hundred (transferred from Salem jail to Madras) had died of diseases of a scorbutic type, such as diarrhœa and dropsy." Speaking of post-mortem appearances, he says: "General dropsy and a tendency to serous effusions into the cavities of the pericardium, thorax and abdomen are the only evidences, as indeed are the other symptoms just noticed (*i.e.*, decay of vital powers, dyspepsia and ulceration of the large intestine), of an impoverished condition of the blood—of a vital fluid deficient in reparative or plastic material." In the Indian famine of 1877–78 this officer was Sanitary Commissioner for Madras. The *British Medical Journal* of that period praises "the boldness and honesty with which . . . he resisted the measures of Sir Richard Temple, the famine delegate of the Calcutta Government—measures which at one time threatened to destroy more people than the famine." The main point at issue between Temple and Cornish was Temple's contention that the natives grew fat on his reduced relief-ration. Cornish, in his official reply to Temple's minutes, exposes the famine-delegate's uncritical observation: "Even in the weight test some caution is necessary, for many of the people who come into camps appear to be filling out and fattening, when in reality they are getting dropsical and in a fair way to die." Cornish observed this form of dropsy under yet another set of conditions. "In 1872 a detachment of native troops was sent from Burmah to occupy a post of the Arracan river in co-operation with the Lushai expedition. The men had no market at hand to buy animal food, and in attempting to live on their rations they sickened and died in large numbers." He gives the hospital admissions as 901 and the causes of deaths as 12 from dropsy and 3 from debility, out of a total of 27.

Porter also described the dropsy of the Indian famine of 1877–78. He was in medical charge of a famine relief camp in the Madras Presidency. He admitted to hospital 3,250 persons, of whom 1,117 died. "Taken as a whole, these patients were emaciated, the majority had œdema of the feet and about 10 per cent. suffered from general anasarca . . . in no case were there marked symptoms of scurvy present." Porter gives the following careful analysis of 22 cases of dropsy occurring in 459 autopsies:—

	Men.	Women.	Children.
Anæmia	3	2	3
Cirrhosed liver ..	4	–	–
Bright's kidney ..	3	1	–
Heart disease ..	3	3	–
	13	6	3

He says: "The surface of the heart was devoid of fat . . . the fat was replaced by œdema . . . There was œdema of the mesentery present."

During the siege of Paris (1870–1) Professor d'Espine says that "œdema was regarded as the first stage of scurvy; but evidently this was not correct. The number of deaths without scorbutic phenomena justified the view that famine œdema was a morbid entity."

Although it has been suggested that " epidemic dropsy," as described by Macleod, Manson and others, is identical with famine dropsy, this is probably not the case. Macleod, in his account of epidemic dropsy in Mauritius, states that " this dropsical disease was by no means confined to the impoverished and sickly." It is possible that Macleod's cases were due to ankylostomiasis.

In the interval between the Indian famine of 1877–78 and the war of 1914 famine dropsy fell out of recognition and was practically forgotten, save for Greig's investigations. Greig's account of epidemic dropsy in Calcutta shows that it differed from war œdema or famine dropsy in material features, notably the frequent presence of cardiac symptoms and the relative frequency of emaciation.

The first recorded appearance of this form of dropsy during the war was at Lille in October 1914. This unhappy town was in German occupation, and the large industrial population was suddenly stripped of everything so that many of the inhabitants had nothing to eat except potatoes. This dietary produced many cases of a general anasarca unaccompanied by albuminuria. Fontan's account of the epidemic corresponds in every detail with famine dropsy. Early in 1915 the disease appeared in prison camps in Germany, associated with various epidemic diseases such as relapsing fever, dysentery, malaria and typhus. At the same time it was observed among the civil population in famine-stricken Galicia and Poland. Thenceforward the disease was reported frequently and from many parts of the Central Powers, as well as from neutral countries. Throughout the prison camps of Germany and Austria, and especially in the so-called " reprisal " camps and companies of prisoners in the hands of the Central Powers, famine dropsy was continually seen.

Accurate statistics as to the relative frequency of famine dropsy in any given community are difficult to obtain. During the war it was practically unknown in the British Army until after the armistice, when many cases were seen among British prisoners released from German camps. These were soon cured by ordinary care and feeding. There were no deaths reported as the direct result of hunger œdema, and there was little opportunity for studying the condition. The following analysis of the disease is, therefore, based almost entirely on a review of papers published previously to the war or of observations made on the abundant clinical material that was available in Austria and Germany.

Captain Park, of the Canadian Army Medical Corps, saw 400 cases whilst himself a prisoner of war between June 1916 and January 1918, but the total number of prisoners amongst whom these cases occurred is not known.

Versmann, who was a director of food distribution in Germany, confirmed the diagnosis only 200 times in a total of 200,000 applicants. Malloch says that of the first 300 consecutive admissions of released prisoners of war to No. 3 Canadian General Hospital about 20 per cent. showed some œdema of the feet, and in some of these there was also swelling of the face about the eyes. None of these cases had albuminuria, the blood pressure was not abnormal, and there was no myocardial insufficiency to account for it. It is interesting to compare with Malloch's estimate the figures given by Porter in the Indian famine of 1877–78 and quoted above.

Von Jaksch reports that in 1917 in Bohemia 22,842 persons were discovered suffering from hunger œdema, of whom 1,028 died. Kraus speaking of Germany as a whole says, "You could count the cases by thousands and the death rate in some places rose to 50 per cent. of the cases," but he gives no exact figures.

Hülse found in certain companies 47·4 per cent. affected. Enright collected 300 cases of œdema in No. 2 Prisoners of War Hospital, Cairo, but many of his cases were suffering from concurrent diseases, notably pellagra, dysentery and malaria, and scorbutic symptoms were frequently present. Moreover, out of 54 cases which he selected for special investigation only two had normal urine; "albumen was almost invariably present."

Captain Gerrard reported the concurrence of some undoubted cases amongst Turkish prisoners of war at Heliopolis, but does not quote numbers.

All observers agree that in the civil population men are affected out of all proportion to women and children. Jansen gives the relative incidence in certain civil institutions as 12·15 per cent. men, 1·2 per cent. women. In the Indian famine of 1877–78 Cornish and Porter recorded a great preponderance of men affected. Lichwitz gives the sex-incidence in a group of 144 cases as 103 men, 39 women, and two children.

As regards mortality, Von Jaksch's figures deal with the largest number collected by one observer. He records 1,028 deaths out of 22,842 cases or 4·5 per cent. Gerhartz described 21 cases with 3 deaths, and Bigland 24 cases with 8 deaths. Park in 400 cases says "about 20 necropsies" were performed. Hülse in 145 cases saw no deaths directly attributable to hunger œdema; death was always due to some concurrent or intermittent malady.

Ætiology.

The chief exciting cause of famine dropsy is long-continued underfeeding. Complete starvation leads to death in eight or ten days without the appearance of dropsy. As already noted, when the daily food ration contains between 800 and 1,200 calories, and these calories are drowned in a fluid nourishment which includes 15 per cent. and more of indigestible cellulose with very little fat and a maximum daily allowance of 50 grammes of protein, then dropsy occurs. It occurs more readily if the victims of such a dietary are men called upon to do hard work and exposed to cold. Undoubtedly climate plays a part, but, as the Indian famine of 1877–78 demonstrated, famine dropsy can occur in hot climates as well as cold. In the war of 1914–18, however, it was seen that in a given community fed on the same ration more cases occurred in cold weather than in warm.

The ingestion of fluid in large quantity is a contributing factor. The German ration for prisoners was very poor in protein and practically fat free. The form in which it was given was almost entirely soup, to which the men were in the habit of adding a great deal of common salt. A large amount of fluid was therefore drunk to obtain a small amount of nourishment, and with this an increased load of sodium chloride was taken.

The nature and source of the water supply have no bearing on the production of the disease. Soil and race have little influence. It was said that the British prisoners of war suffered less on the same ration than Russians, Roumanians or Serbians, but the parcels of food sent to the British from home increased their prison diet particularly as regards calorie-content.

Exposure and fatigue hasten the onset of the dropsy ; whilst previous illnesses such as diarrhœa and dysentery so constantly precede it that at one period of the war it was suspected that the disease might be due to an infection transmitted through the alimentary canal.

So far as dropsy was observed in the civil populations of the countries where general food-shortage existed, it affected always the poorest first and in greatest numbers. Men between the ages of 40 and 50 developed the disease most readily ; women and children were less frequently affected, and then only in such households as lived in the direst poverty. It is probable that a diet rich in water, sodium chloride and alkalies is only a causal factor in so far as it is low in calories. Hindhede does not think that absence of fats from the diet is of great importance ; he says that in Denmark by April 1917, "after nine months' experience with a fat-free diet we were convinced that adults could live without fats, provided they were given greens." Yet he mentions elsewhere that during the war the diet of the Danish people consisted chiefly of milk, vegetables and bran. Where famine dropsy appeared milk was nearly always absent from the dietary.

Symptoms.

Famine dropsy is characterized by four cardinal symptoms, œdema, polyuria, bradycardia and asthenia. The onset is gradual. After a few days' malaise, during which the patient complains of little beyond great lassitude, physical weakness, headache and a noticeable increase in the quantity of urine passed, there appears an œdematous swelling of the limbs and trunk. Sometimes the nature of the swelling is so unmistakable that the patient diagnoses his own case as dropsy.

The œdema begins in the feet, ankles and dependent parts, and often extends over the whole body even to the hands and face. Ascites, hydrothorax and hydropericardium are of common occurrence. The skin assumes a pale yellow tint, muscular wasting may become extreme, and there is usually very marked apathy. Night blindness and xerosis of the cornea have been reported, but, since night-blindness may occur in any state of exhaustion or mal-nutrition if the retina is exposed to a bright light, it cannot be considered as a diagnostic feature of famine dropsy. When with appropriate treatment the dropsy disappears, the emaciation begins to be obvious. This emaciation is an integral part of the disease and is always very great. It corresponds in fact with the total loss of subcutaneous and other fat revealed by autopsy, and is a main point of distinction between famine dropsy and that due to renal or cardiac disease.

At the first onset of œdema a remarkable polyuria is invariably observed. It takes the form of nocturnal frequency (nykturia) sufficient to interfere seriously with the patient's sleep. Enuresis is not uncommon. The heart's action becomes very slow; extreme bradycardia without irregularity occurs in almost all cases. The rate is usually between 40 and 50 per minute, but a rate of 26 has been recorded. This bradycardia is of sinus origin. The heart sounds are faint and muffled; sometimes a soft systolic bruit is heard over all the valvular areas. The pulse becomes small and feeble, the blood pressure low (90–100 mm. Hg). The lungs are as a rule normal, unless there is a considerable degree of hydrothorax, or some complicating broncho-pneumonia. Usually there is a striking absence of dyspnœa, cyanosis and the other signs of failing pulmonary circulation. The liver and spleen are not enlarged. There are no changes referable to the nervous system. Scorbutic manifestations are conspicuously absent except in those cases where scurvy co-exists. The skin changes of pellagra do not occur in uncomplicated cases of famine dropsy. The temperature is normal or subnormal. Fever, if present, depends upon some complication.

Diarrhœa is a symptom so constantly present as to raise considerable question whether it may not be a causal factor. There seems an undoubted relation between the indigestible residue of the food and the diarrhœa. Hülse has shown, moreover, that owing to this indigestibility there is a constant waste of calories in the fæces notwithstanding the general calorie-deficiency and the body's urgent requirements. Park suggests on good evidence that this diarrhœa is sometimes at least non-infectious. In support of this view Maase and Zondek point to the absence of pain and tenesmus, to negative rectoscopic appearances, and to the absence of pathogenic organisms, especially those of dysentery, from the stools. It remains uncertain whether this diarrhœa is due to the mechanical irritation of indigestible residue, to excessive excretion of water by the mucosa of the bowel, or to the actual food-deficiency which is the cause also of the œdema. Maase and Zondek observe that during the second half of the epidemic in 1917, about May or June onwards, diarrhœa was very rarely seen.

All observers agree that simultaneously with the first appearance of œdema there is a great increase in the amount of urine and in the frequency of micturition. When as the result of treatment the œdema begins to disappear, there is a second rise in the quantity of urine passed. At no time is there anything in the nature of suppression of urine, in spite of the amount of dropsy present. The polyuria seems to go hand in hand with polydipsia. The urine is clear, pale yellow in colour, with a low specific gravity. The amount secreted in 24 hours may be as much as 3½ to 4 litres—in one case 7½ litres are recorded; it varies directly with the intake of fluid. In true cases of famine dropsy no traces of albumin, sugar or casts are found at any period of the disease. The chief alteration in the composition of the urine upon which various observers agree is a marked increase in the chlorides. As regards phosphates, Rumpel Knack and Neumann report an increase and Maase and Zondek report a decrease. Calcium and magnesium have been found normal or increased.

As regards nitrogen metabolism, the majority of observers agree with Maase and Zondek that there is no constant abnormality. The total nitrogen corresponds with the low protein value of the diet, and the urea-nitrogen is found decreased, but improves with the diet. The ammonia-nitrogen is relatively increased as in all forms of starvation. Amino-acids and kreatinin sometimes show a slight and variable increase, but kreatin is considerably increased, depending perhaps on disintegration of tissue-protein. Hülse and Jansen have observed in some cases a negative nitrogen-balance, and consider that the loss of nitrogen represents a breaking-down of tissue-protein. Maase and Zondek, whose cases did not exhibit a negative nitrogen balance, remark that Jansen's patients had a much lower average protein-intake (50 gm. protein) than theirs (90–100 gm. protein). Urates are as a rule increased in the early stages of the disease. Acetone has occasionally been found in the urine. Jansen states that in spite of the low protein content of the food there is constant nitrogen loss in the fæces as well as in the urine. He is inclined to attribute this to impaired digestive powers. Franke and Gottesmann attributed the condition to a nephritis without albuminuria. They claim to have found the renal function impaired on testing with phenol-phthalein. Practically all other observers disagree with them and have found the renal functions normal. The only constant alteration in the urine is the increased output of water and chlorides.

Hydræmia is constantly present, but the hydræmia does not correspond with the degree of œdema. The specific gravity of the blood is commonly between 1,047 and 1,052 ; the lowest recorded is 1,038, and in this case there was only slight œdema, The specific gravity of the serum ranges from 1,021 to 1,027, the minimum being 1,014. The osmotic pressure of the serum as measured by depression of freezing point (Δ) is from $-0{\cdot}54$ to $-0{\cdot}58$. Viscosity and electrical resistance remain normal.

The number of erythrocytes may vary within wide limits (1,000,000 to 5,300,000). In the majority of cases there is a moderate degree of oligocythæmia (3,000,000 to 5,000,000). The hæmoglobin index is normal. In cases with less than three million erythrocytes cell changes have been observed ; basophilic granules with polychromatophilia, a slight degree of poikilo and aniso-cytosis, and in a few cases normoblasts.

In general, leucopenia is present. The number of leucocytes commonly lies between 2,000 and 8,000 per c.mm. Where the count is above 8,000 some complication may be suspected. There is a relative decrease in neutrophiles, and a relatively large number of immature (Arneth) cells amongst them. Eosinophiles and basophiles are often increased ; but the chief alteration is an increase in mononuclears, mainly large mononuclears of which the proportion may reach 55 per cent. These cells frequently attain a very large size, six or seven times that of the erythrocytes; there are numerous coarse basophile granules in their protoplasm.

Corresponding with the hydræmia there is a constant and definite fall in the total proteins of the blood serum. The relative proportions of the nitrogen constituents agree with those found in the urine. Urea-nitrogen is low, but increases with the protein-intake; ammonia N. and kreatin are increased; amino-acid N. and kreatinin are variable, and never more than slightly increased. In many cases there is a high degree of acetonæmia. Although there is frequently so great an increase in the chlorides of the urine, Maase and Zondek have found the sodium chloride content of the blood practically normal. The blood-sugar is said to be deficient during the stage of hydræmia and increased as the œdema subsides. Maase and Zondek point out that the sugar-content corresponds with normal blood, whereas in renal and ascitic dropsy there is hyperglycæmia without glycosuria. The lipoid-phosphorus is greatly decreased in the serum, whilst the acid-phosphates are increased. The lecithin-content of the erythrocytes is diminished, the cholesterin remaining unchanged. The fat-content of the serum has been found normal by Gerhartz and diminished by Hülse, Knack, and Neumann. Maase and Zondek have recorded the following analysis of the transudate compared with that of renal and hepatic dropsy:

	Famine Dropsy.	Renal Dropsy.	Cirrhosis of Liver.
Albumen per 100 c.c.	0·116	0·343	0·941
Amino-acid N ,,	0·0028	0·0150	0·0112
NH_3N	0·0170	0·0085	0·0068

These figures show the same hypo-albuminosis and increased NH_3N as have been observed in the blood and in the urine.

Pathology.

The problems of œdema formation as a whole are so little understood that it is impossible at present to offer any conclusive explanation of the pathogenesis of famine dropsy Clinical œdemas are of three types:—

(i) The inflammatory œdemas, in which the fluid permeates the cells of the inflamed area and does not move to other parts of the body under the influence of gravity.

(ii) The nephritic œdemas, in which the fluid is more or less loose in the subcutaneous tissues and more readily changes its position, are accompanied by excess of water in the blood with a corresponding increase of sodium chloride, the percentage concentration of chloride in the blood remaining unchanged, but that of the other constituents being diminished.

(iii) Cardiac œdemas, which are also hypostatic, but are unaccompanied by changes in the relative amount of water and sodium chloride in the blood.

But in all forms of œdema recent observations tend to the view that some local damage to the capillary endothelium exists. So far as famine dropsy is concerned no histological evidence has been obtained of damage to the capillary walls. It may none the less exist. This hypothetical damage to the capillary endothelium may be either a nutritional defect, or a toxic lesion. In nephritis the latter seems clearly proved. Maase and Zondek are of opinion that in famine dropsy the toxic elements play a secondary part. They conjecture that increased protein disintegration gives rise to toxic products comparable to Volhard's nephroblabtine in renal œdema. It is more probable that some nutritional defect alters the permeability of the capillary walls. In this connection the deficiency of lipoids in the blood seems an important factor. For this the absence of fats from the food must bear the principal blame. Experimentally, Harden and Zilva produced œdema in monkeys fed on a diet deficient in fat-soluble A, but the diet was also deficient in fat as a whole.

Apart from these two factors, toxic and nutritional damage to the capillary walls, three other possible causes may be at work. These are, firstly, the altered composition of the blood, which exhibits hydræmia, hypoalbuminosis and deficiency of lipoids. There may be, as a result, an increased passage of fluid through the capillary wall. But the blood changes appear to be of too slight a degree, and this theory is also incompatible with the rapid resorption of the œdema. Secondly, there is Fischer's theory of œdema that the tissue-cells damaged by nutritional defects become capable of excessive imbibition of water. There is no evidence in support of this theory, while the fact that the fluid in œdema gravitates from one part to another and can sometimes be drained off by hollow needles proves that cell-imbibition is not the essential factor. Finally, there remains the theory that the endocrine glands are in some way responsible. Eppinger has suggested that the thyroid gland controls the water-economy. With a little more probability and supported by experimental findings, McCarrison conjectures that the œdema of beri-beri is connected with the excessive production of adrenalin. The total adrenal-content of the hypertrophied adrenal glands in cases of experimental beri-beri in monkeys greatly exceeded the amount found in healthy animals. Enright failed to find hypertrophy of the adrenal glands at autopsy in cases of death with œdema amongst Turkish prisoners of war in Cairo, but, as pointed out previously, he does not appear to have been dealing with famine dropsy.

Other causal factors have been suggested, which may be briefly considered.

Mere excess of fluid in the diet undoubtedly cannot account for the dropsy. Life can be supported on fluid diet without the appearance of œdema, provided there is a sufficiency of protein, calories and vitamines. In the polydipsia and polyuria of diabetes mellitus and insipidus the mere ingestion of fluid does not produce dropsy.

With regard to the supposition that an excessive intake of sodium chloride is a causative factor, although an excess of common salt may have been a contributory factor amongst prisoners of war, it is not essential to the production of famine dropsy, as proved by Harden and Zilva's experiments.

With regard to the influence of food deficiencies and absence of vitamines, Kohman, who produced œdema in rats fed on a diet composed largely of carrots, found that the addition of fats, or fat soluble A, or increase in salt-content of the diet, had no noticeable effect on the occurrence of the œdemas. But there was much more marked œdema where there was much water in the diet than when the animals were on a dry diet.

There seems little doubt that protein-deficiency plays a part in the production of the disease. Cornish, in his observations on prison dietaries and Indian famines constantly attributed the appearance of dropsy to inadequate nitrogenous, rather than non-nitrogenous food. Denton and Kohman have stated that dropsy occurs in rats fed on a carrot diet, when the proportion of nitrogen is reduced by the addition of some non-nitrogenous food-stuff, such as fat or starch. Maver has confirmed these observations, and concludes that the disease is not a specific vitamine-deficiency disease, but is in a broader sense a " deficiency " disease, resulting from a protracted existence on a diet poor in total calories and especially in protein.

The most striking feature in all autopsies is the total absence of fat throughout the whole body. At the normal sites for fat deposits, in the subcutaneous tissues, in the omentum and mesenteries, about the kidneys and on the heart, fat is replaced by œdema, producing a translucent gelatinous tissue. Hydropericardium, hydrothorax, and ascites are frequently seen.

The heart is in all cases greatly atrophied, the muscle pale and flabby exhibiting histologically the changes of brown atrophy. There is increase of pigment at the poles of the cell nuclei, without true regressive changes. In spite of these changes in the muscle, dilatation and hypertrophy do not occur, and the valves remain healthy and competent. The lungs appear small, retracted, anæmic and soft. Sometimes there are patches of atelectasis at the margins. Bronchopneumonia and pulmonary œdema are common.

The liver is, as a rule, small and like the kidneys and spleen pale and soft. Hülse found that no histological changes were constant in the liver and kidneys beyond much and varied fatty degeneration. Jansen found no trace of fat in the liver cells when stained with Sudan red; glycogen, too, was absent from the liver cells. The kidneys are healthy; histologically the epithelium and tubules are intact, and it has been particularly noted that the renal tubules are of normal width and without thickened walls.

The spleen shows remarkably few follicles; the trabecular stroma and the vessel sheaths stand out very clearly from the atrophic pulp. Fibrous induration has been observed round the follicles. On the whole, no such regenerative processes as are seen in general infections, especially relapsing fever, were found.

Histologically, not only is fat absent from the tissues of all organs and muscles, but the muscle-fibres, like the liver cells, are totally devoid of glycogen.

Evidences of concurrent or intercurrent disease are frequently met with, particularly tuberculosis and inflammatory or ulcerative affections of the large intestine. Park regards these changes in the large bowel as an integral part of the disease not necessarily due to any specific infection. He was struck by the fact that, although this form of diarrhœa was rife in the prison camps, and the sanitary arrangements were favourable to the spread of intestinal organisms, yet the better-fed prisoners were scarcely ever affected.

Diagnosis.

The diagnosis of famine dropsy rests chiefly on the exclusion of other diseases. The presence of albuminuria and casts in the urine may be taken as evidence of renal disease, but their absence does not prove that the kidneys are healthy. According to Fontan, persons with damaged kidneys may be the first to develop dropsy as the result of underfeeding with a dietary mainly liquid and rich in common salt.

Famine dropsy differs from cardiac œdema in the slowness and regularity of the heart's action, in the absence of signs of cardiac dilatation, and in the absence of dyspnœa and cyanosis. Peripheral neuritis, even in its slightest manifestations such as pains in the legs and paræsthesia, suggests beri-beri rather than famine dropsy.

Ankylostomiasis presents considerable difficulty in differential diagnosis; the presence of eosinophilia will suggest the necessity for careful investigation of the fæces. Pellagra should be recognised by its characteristic skin changes. Scurvy and famine dropsy so frequently co-exist that it is almost impossible to distinguish where the one begins and the other ends. It is clear, however, that the hæmorrhages of scurvy are not essential symptoms of famine dropsy.

Pre-disposing, concurrent, and intercurrent diseases are so commonly met with that they should always be specially looked for. The most frequent, and the most important from a prognostic standpoint, are tuberculosis, malaria, and dysentery. The relation of diarrhœa to famine dropsy and dropsies of inanition is interesting and at present not clearly understood. Park's comment is worth quoting in full: " A common complication of this œdema in my experience was a diarrhœa with frequent watery stools, containing blood and mucus intimately mixed. The post-mortem findings showed much hyperæmia and thickening of the lower bowel, with occasional ulceration. Although so common amongst these patients as to suggest that it was an infectious dysentery, I did not believe that it was the result of any specific organism, for we scarcely ever found it among the better-fed prisoners, although the sanitary arrangements were such as to give great scope to the spread of intestinal organisms." There is a possible parallel with this in Edgeworth's observations " on the occurrence of general subcutaneous non-renal œdema as a familial affection," where in the description of the death of five out of six infants in one family with general œdema following upon diarrhœa he says: " It is well known that dropsy, especially of the face and extremities, may occur in infants suffering from chronic diarrhœa without albuminuria." McCarrison states emphatically that " the food deficiency is the primary cause of the diarrhœa or dysentery as much as of the deficiency disease syndrome."

Famine dropsy and inanition œdema seem at present inextricably mixed. The essential conditions which lead to famine dropsy pure and simple are, however, well established —namely, prolonged underfeeding with a largely fluid diet poor in calories, combined with exposure to cold and hard physical exertion.

Prognosis.

On the whole, the prognosis in famine dropsy is good, provided that treatment, in the form of improved diet, can be given. According to Von Jaksch, three considerations affect the prognosis in favour of the patient, namely, youth, early treatment, and freedom from any other disease, especially tuberculosis. Old people and infants fare worst. Budzynski and Chelchowski place the death rate in persons over 40 years of age at 18·3 per cent., and in children between three and four years old at from 22 to 33 per cent. The mortality is greater in men than in women. This observation relates not only to cases which occurred in 1914–18, but to all previous records of famine dropsy.

Uncomplicated cases usually recover with rest in bed and an increased diet. Relapses, however, are common when the patient first gets up and begins to exert himself. Malloch states that the œdema cleared up within 24 to 48 hours following rest in bed and ordinary diet, but he adds that at first the œdema was only absent if the man stayed in bed all day, and it was some time before he was able to get up without a return of the œdema. It is not known how long these men took to regain full physical efficiency, because their subsequent history in England was not traced.

Treatment.

The treatment is simple. Rest in bed, warmth and a diet rich in carbohydrates will cure most cases in a short time. The diet at first must be light, easily digested, and given in small quantities as in any case of starvation. The amount of liquid and of common salt should be limited. Attention must be paid to any other disease that may be present. Relapses of diarrhœa are apt to be troublesome. Park lays particular stress on the value of cod liver oil. Emphasis must be laid, however, on the most recent researches, which demonstrate that an adequate protein-content is no less essential to the dietary than an adequate supply of calories. The prevention of famine dropsy consists in maintaining a diet consisting of at least 2,000 calories, and this calorie-content is only compatible with light work. The experience of Hindhede in Denmark shows that green vegetables and milk can supply the deficiency of fats, starches and sugar. The minimum daily nitrogenous intake necessary to avert dropsy has not yet been established, nor the part played by vitamines. It is abundantly clear that in future the estimates of minimum food requirements must take into consideration the indispensability of each and all of the food factors known and unknown. The researches of Sherman fix the minimum biological value of protein in the daily diet at approximately 45 grammes for a man of 70 kilograms weight, although Hindhede fixes it at the much lower figure of 27·5 gm. for the same body weight. Bayliss, in referring to Hindhede's experiments, remarks that "care was taken that the total caloric value of the food was abundant, a point of essential importance."

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CHAPTER XXI.

PELLAGRA.

If defined as "a disorder of metabolism with periodical manifestations characterized by gastro-intestinal disturbances, skin lesions, and a tendency to changes in the nervous system," this disease was first recorded as such in Spain during 1735.

Its heaviest incidence has fallen upon European countries which border the Mediterranean and lower Danube; when looked for by experts, cases have been found as far north as the Shetland Islands.

At the onset of the war, theories regarding its ætiology were divisible into two main groups—the dietetic and the infective. Holders of the former view were turning from search in cereals, especially in maize, for a hypothetical toxin, and were inclining to the American ætiological theory of food deficiency. Exponents of the latter theory had recently suggested that there might be an insect-vector, such as *Stomoxys calcitrans* or some species of *Simulium*.

An outbreak of pellagra among Turkish prisoners of war in Egypt afforded unique opportunities for research upon a scale, and under favourable conditions, such as could hardly obtain in a civilian community. A special investigation was completed on 31st December, 1918, and upon the conclusions then reported is based the following account of pellagra from the military standpoint.

The committee of enquiry consisted of two members—Colonel F. D. Boyd, consulting physician to the Egyptian Expeditionary Force, and Lt.-Colonel P. S. Lelean, the A.D.M.S. for Sanitation, having as collaborators recognized experts in bromatology, bio-chemistry, pathology, bacteriology, protozoology and hæmatology.

Incidence and Distribution.

The monthly per mille incidence, as recorded by the hospital admissions of all prisoners of war suffering from pellagra, from the first cases in November 1916 to the end of 1919, is shown in Chart I.

The maximum corresponds to 1,540 cases admitted to hospital in November 1918, and the total for the charted period amounts to 9,257 cases—or 8·5 per cent. of all prisoners captured.

Amongst British and Indian troops comprising the Egyptian Expeditionary Force, with a maximum strength of 316,605, there occurred, so far as is known, only a single and doubtful case: an Indian was diagnosed, but was repatriated before the uncertain diagnosis could be established. British garrisons in Egypt, where pellagra is rife among the *fellahin*, also remained unaffected.

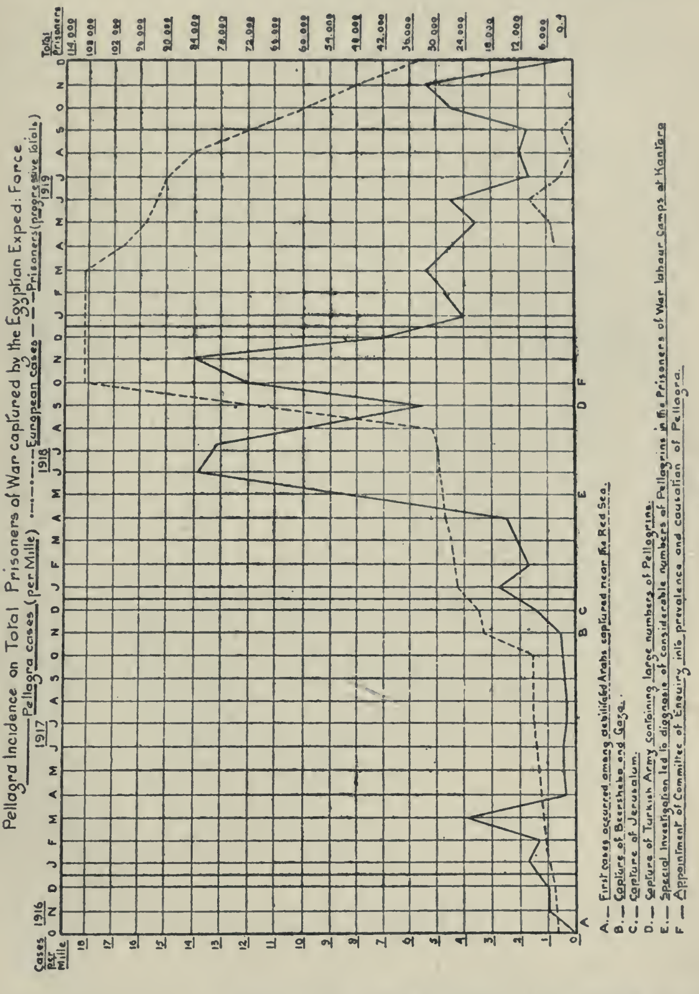

CHART I.

Among men of the Egyptian labour corps, drawn from highly pellagrous districts, the prevalence of this disease was such that 245 cases were found in one actively working gang of 1,000 labourers. This affords a most striking contrast to the immunity of British troops, beside whom throughout the war thousands of these men worked by day and camped by night.

Among German and Austrian prisoners, some of whom had been in captivity for two years, no case had been reported up to 31st December, 1918, when the special investigation was completed.*

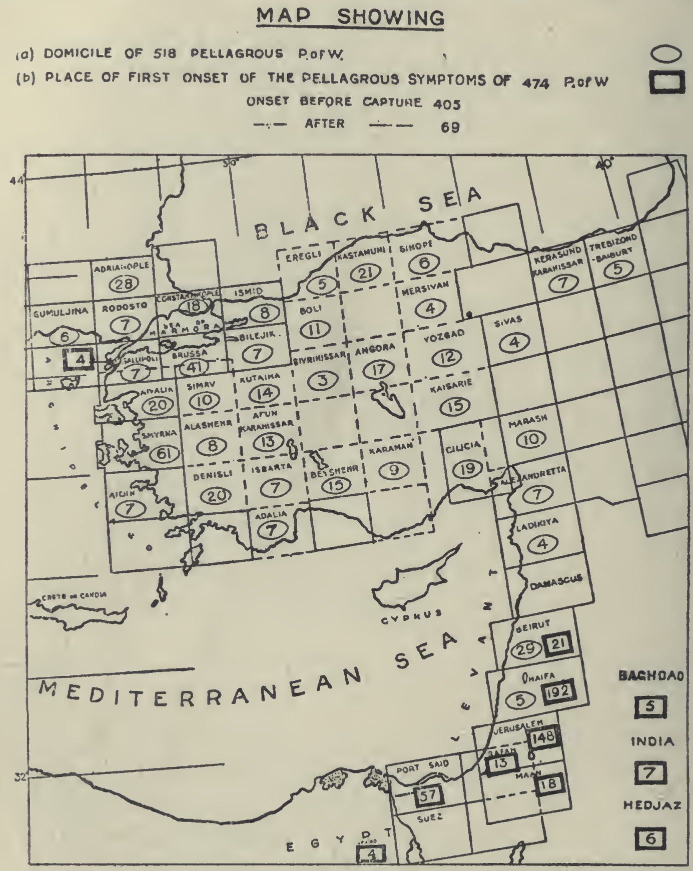

FIG. 1.

Among 518 unselected pellagrins, enquiries were made regarding the areas in which they were enlisted and the districts in which they were when the initial pellagrous rash, with which these aggregated patients were thoroughly familiar when questioned, appeared.

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* Cases which have occurred since that date will be referred to later. The original heading of "Europeans," with sub-headings "Germans" and "Others," having afforded "nil" returns for so long, the sub-headings were eventually omitted for a time and only revived during April 1919. The per mille rates since then—the only official figures available—are included in Chart I.

That a definite onset was common was suggested by the fact that 474 of these men (91 per cent.) were able to give a date and locality. The results of this enquiry are shown in the map on the opposite page.

With reference to the possibility of these cases dating back to the areas in which they were enlisted, it is noted that only one stated that his rash preceded his enlistment, while only five had seen similar rashes among their acquaintances before the war. Moreover, only one of the many captured medical officers of all nationalities and from many districts had seen a case of pellagra in his practice—a Damascus practitioner who had seen five cases in thirteen years. While the tendency to overlook cases in temperate climates is recognized, it is justifiable to conclude that its prevalence in Turkey before the war was slight.

The facts which call for special notice are that cases began to occur in Gallipoli; that the map, taken in conjunction with dates, indicates a great preponderance in those vilayets where the Turks were aggregated towards the end of the war; and that there are sufficient cases to show that troops on the Mesopotamia front were also affected.

Cases which denied any previous symptoms were admitted to hospital from all prisoner camps, whether in the wooded and watered Palestine plain, the arid desert bordering the Suez Canal, the cultivated land beside the Nile at Maadi, or by the seaside at Alexandria. At first it was thought that the labour camp at Ludd, Palestine, was free, but when 1,840 prisoners were transferred thence to Kantara, where medical officers with greater experience in diagnosis were available, 122 pellagrins from among their number (6 per cent.) were admitted to hospital for pellagra within 48 hours of their arrival.

Of 484 prisoners, unselected, who were able to give an approximate date for the onset of symptoms, 85 per cent. were pellagrous before capture. Of the 359 able to fix a definite date within six-monthly periods, this date was :—

From 12 to 6 months before capture in 40 cases (11·1%).
,, 6 ,, 0 ,, ,, ,, ,, 279 ,, (77·8%).
,, 0 ,, 6 ,, after capture in 27 ,, (7·5%).
,, 6 ,, 12 ,, ,, ,, ,, 13 ,, (3·6%).

The discovery of 236 definite cases in one batch of 1,300 prisoners (18 per cent.) examined in October 1918, on the day after their arrival direct from the front, confirmed the belief that pellagra in prisoners had usually occurred before their capture.

The conclusions drawn from these facts are that pellagra among the Turkish forces was a result of the war; that it was due to a cause progressively increasing in intensity towards the end of the war; and that this cause became abruptly less active coincidently with capture.

As regards the incidence on Turkish military formations, 51 divisions and 6 corps troops were represented among 505 consecutive pellagrins. While one division provided 53 cases, 33 other divisions only provided 54 cases among them—with a maximum of 4.

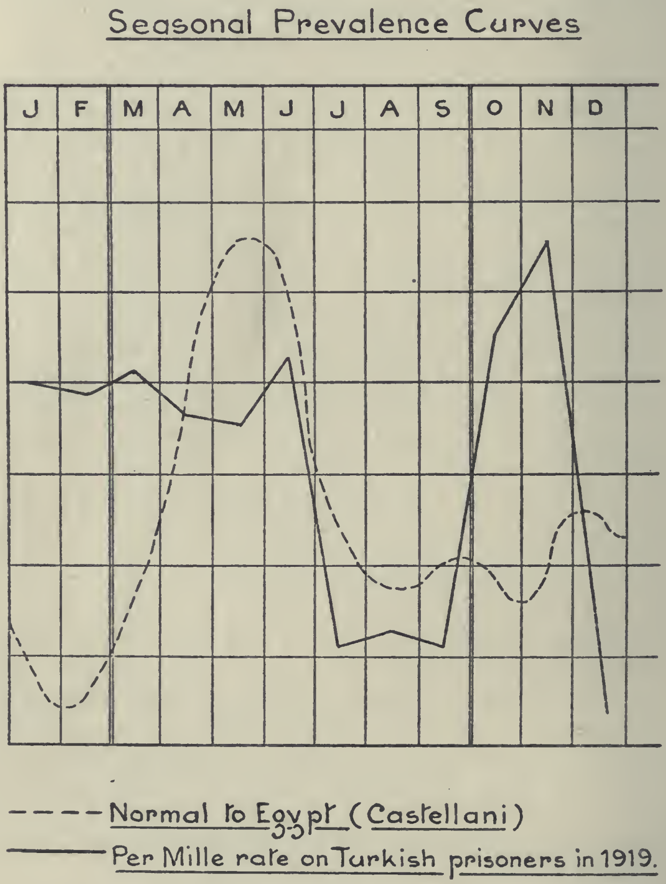
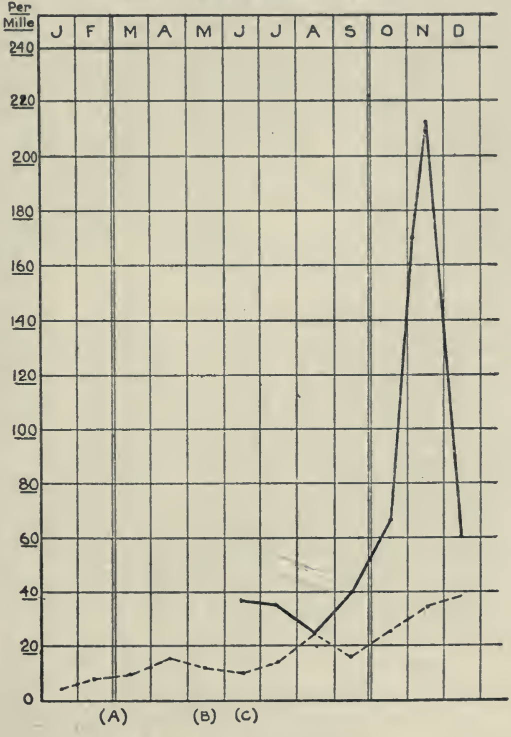


Chart II.

This clearly indicates that the essential factor in causation was of wide spread application, and affords evidence that pellagra is not infectious from case to case.

In relation to social grade, although several admissions occurred from the officers' prisoners of war camp at Alexandria during 1917, that camp reported no new case and only three recurrences in 1918, during which year the strength rose from 1,900 to 4,400. Incidence was thus markedly lower upon the officer class than upon the rank and file. Rations were identical; but officers supplemented theirs, other ranks could not do so.

Pellagra incidence on labour and non-labour Turkish prisoners in 1918.
—— Labour (average strength 5000 approx).
- - - Non-labour (average strength 25,000 approx).



(A). Strength increased from 900 to 6000.
(B). a relatively high sick rate occurred.
(C). The first diagnosis of Pellagra was established.

CHART III.

In 1917 the prisoner population was small; in 1918 it was subject to abrupt trebling. The per mille ratios for 1919 are, therefore, adopted for preparing Chart II of the seasonal prevalence for purposes of comparison with the curve of normal Egyptian prevalence as given by Castellani in actuals.

To restrict the population dealt with to those present from the beginning of 1919, there are excluded from the chart 12,600 emaciated prisoners who had been besieged at Medina for many months. On arrival in Egypt in February and March 1919, these had 58 pellagrins among them, and 275 others were admitted for that disease within a short period.

In 1919 practically no fresh cases were admitted on the diet then in use, the admissions in that year being recurrent cases.

With regard to the relation between pellagra incidence and labour, pellagra was first diagnosed in the chief Turkish prisoners' labour camp, which was at Kantara, when the high sick-rate there during May and June 1918, led to the special investigation. The importance of this factor is indicated by the comparison shown in Chart III between the incidence in this camp and that in four other camps, where Turkish prisoners were not employed as labourers, but where, after careful medical inspection by an officer with special expert knowledge of the disease, they were being enlisted as paid labourers previous to their transfer to the chief labour camp.

The Kantara labour camp was close to British and Indian units, on clean and absolutely barren sand, over a mile east of the Suez Canal, and under extremely good sanitary conditions. During the day the labourers worked in gangs about the camp on duties involving a maximum energy expenditure of some 80,000 kilogramme metres a day. This work was in no way exacting, nor liable to be excessive. The energy expenditure was only two-thirds that of Egyptian hard-labour convicts. Of 100 pulse-rates taken immediately on the men's return to camp after the heaviest labour observed, only two failed to return to normal after 15 minutes' rest, and both these men were found to have slight fever although refusing to go sick.

In spite of these favourable conditions, men transferred to this camp, after selection by the most experienced pellagra experts as free from suspicion of the disease, rapidly became pellagrous after starting work, although the troops beside them remained wholly free.

If allowed to continue at work—at their own request—they became hospital cases within about eight weeks of onset of the initial diagnostic symptoms; if placed in hospital as soon as the diagnosis was confirmed by experts, they recovered so rapidly that in many cases the symptoms subsided almost to vanishing point in the few days that elapsed pending their transfer to Egypt, the only treatment being rest and dieting.

The total admissions for pellagra were 1,540 out of a total prisoner strength of 109,000, and in November 1918, no less than 1,067 of the hospital admissions for pellagra came from this camp with a strength averaging some 5,000 Turkish prisoners.

Symptoms.

The characteristic symptoms of a developed case are dryness and wrinkling of the skin, with pigmentation over the whole body, but more especially over the face, neck, arms and hands, but the symptoms in general conformed to the usual text-book descriptions of the intestinal, cutaneous and nervous manifestations of the disease. Certain symptoms, however, observed in the earliest stages are important for the purpose of diagnosis.

The earliest observable sign was dryness and loss of elasticity of the skin on the dorsum of the hands and wrists. Later, it was found that the affected areas, going on to the characteristic pigmentation, remained dry when copious sweating elsewhere followed injection of pilocarpine. Hypo-chlorhydria was also amongst the earliest indications of the disease, and progressed towards an ultimate achlorhydria. Very early, too, there was a notable fall in systemic blood-pressure. A little later there occurred a marked loss of muscle tone and substance, usually appearing first in the upper arm and shoulder-girdle. In the Kantara labour cases this was usually observable within six weeks of the earliest suspicion of a man being pellagrous. Parotitis occurred in a limited number, and œdema of the ankles in a very limited number of cases. Later, pigmentation was likely to affect all scar tissue and pressure areas, even those so little exposed to light as the great trochanters and the zone constricted by waist-girdles.

Indicanuria was common in developed cases, progressed with the disease and subsided as slight cases were arrested. For example, amongst 296 men specially examined, 64·3 per cent. of healthy Turkish prisoners had no indicanuria, and 35·7 per cent. only a slight amount ; whereas amongst pellagrins in the quiescent stage, 54·2 per cent. had slight, and 11·5 per cent. well-marked indicanuria ; while in pellagrins in the active stage, marked indicanuria was present in 28·2 per cent., and slight indicanuria in 64·8 per cent., only 7 per cent. showing an absence of indicanuria.

Treatment.

With regard to treatment and prognosis, general experience indicated that early cases treated by rest and a generous dietary rapidly lost all symptoms of the active disease, although no drugs were exhibited. Advanced cases progressed to a fatal end despite all measures adopted.

Morbid Anatomy.

Among 178 autopsies carried out in prisoner hospitals in Egypt there were only two in which pellagra could be regarded as the determining cause of death ; the fatal ending was almost invariably due to a supervening acute infection such as pneumonia, dysentery, tuberculosis, or malaria. Lesions of former dysentery and pulmonary tuberculosis were also found in 61 per cent. and 17 per cent. of these autopsies respectively, and ascarides were found in 16 per cent.

No reliable estimate could thus be made of the mortality of pellagra in the absence of acute terminal infections of other diseases, the lowered resistance to which is so conspicuous a feature of pellagrins.

Findings at the above autopsies were so obscured by the effects of the terminal complicating infections as to be of negative value, with two exceptions ; the adrenals were found of an average lighter weight, and ganglion cells of the sympathetic nervous system were found in certain cases to be plasmolysed.

Ætiology.

An ætiological theory, to be acceptable, must satisfactorily explain how it came about that in an army enlisted in, and subsequently occupying, areas where pellagra was previously almost unrecognized, the disease became widely distributed and increasingly prevalent towards the end of a long war, while the incidence abruptly declined on capture and transfer of prisoners to a pellagrous country, but continued to occur in all the widely separated prisoner camps, although the British and Indian troops camped alongside them remained wholly unaffected. Further, why it was that officers were less affected than other ranks, and European far less than Asiatic Turks, and why previously healthy labour prisoners were the most heavily and rapidly affected, but as rapidly recovered on rest and good diet without leaving the working area, must also be explained.

The essential or dominant cause of this outbreak must thus be some factor exclusively or predominantly applicable to the affected prisoners as compared with unaffected British and Indian troops. It is noted, however, that this disease may possibly be due to associated predisposing and determining causes, and that one or both may be operable for a longer period than the two years with which this analysis deals.

Water supplies, climatic conditions, biting flies and special local conditions were definitely excluded as factors inconsistent with the above facts. General hygienic conditions were excluded as they were at their best in the Kantara labour camp, which was most affected. Case to case infection was eliminated because of 480 cases from 150 tents in one compound, 395 were aggregated in a purely chance distribution. Thirty-seven cases corresponded with a greater aggregation in tents and 38 with less aggregation than the average. Of 253 orderlies in the chief hospital treating pellagrins in all stages for over two years not one showed any sign of the disease. No recorded case occurred among the many captured medical orderlies. No evidence of a bacteriological or protozoological infective agent was found in 544 special examinations, among many others, of fæces, blood, urine and cerebro-spinal fluid of patients in all stages and from various camps both labour and non-labour. Helminthic entozoa—although possibly amongst contributory factors—were not considered to play an essential part because non-pellagrous prisoners were as badly infested as the pellagrins, for ascaris was estimated as infecting 63 per cent. of prisoners, and the immune Indian troops were also generally and heavily infested by this parasite.

There remained for consideration the theory, propounded by Professor W. H. Wilson, that pellagra is associated ætiologically with an actual or relative deficiency in the biological protein value of the diets. The biological value of a protein is the ratio which its power to maintain nitrogenous equilibrium bears to that of pure animal protein. The actual minimal daily needs of a standard male are estimated by Wilson as being of the biological value of 40 grammes of protein for no labour or light labour, and 45 grammes for hard labour. The relative value must obviously be diminished if the total calories expended in labour exceed the total energy provided by the diet, as amino-acids on their way to the tissues are then oxidized to make good the immediate energy-deficit. American work by Goldberger indicates that a low protein diet produces pellagrous symptoms in about five months, but it is reasonable to suppose that this period may be modified both by varying intensity of the deficiency and by idiosyncrasy in the power of digesting, assimilating or metabolizing protein. A deficient supply of protein to the tissues may thus be due to faulty diet, defective assimilation, or adverse disparity between energy intake and energy expenditure.

The extent of mal-assimilation of food by pellagrins was specially investigated, comparative groups of healthy and pellagrous Turkish prisoners being segregated and given the same ration food under carefully controlled conditions. In the pellagrous group there was a fæcal loss amounting to 35 per cent. of the ingested protein and 28.2 per cent. of the ingested fat. The further subsequent loss of assimilated nitrogen, by its rapid excretion as indican without having been available for metabolism, has already been referred to.

This leads up to consideration of various dietaries in use by the various bodies of troops and prisoners concerned, with a view to ascertaining how far this theory affords an adequate explanation of the occurrence and distribution of pellagra among the troops.

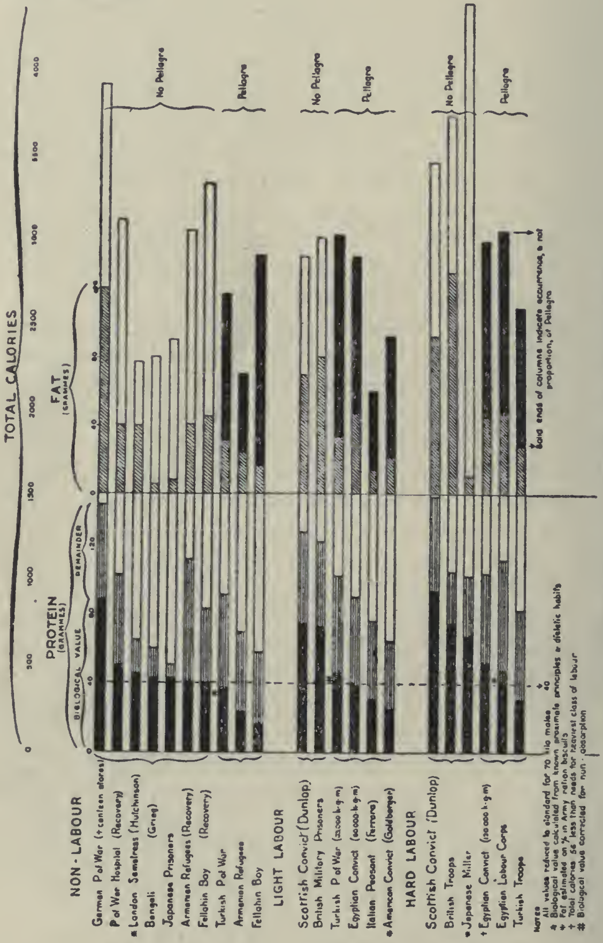


FIG. 2. DIETETIC VALUES IN PELLAGRA

The above graph and following table give the data from which conclusions may be drawn. The graph indicates that the only dietetic factor in this wide variety of diets, which constantly correlates pellagra incidence, is the biological value of protein (B.V.P.). The table gives the estimated amount of grammes of each constituent daily.

	Protein.		Fat.	C.-Hy.	Calories
	B.V.P.	Gross.			
BRITISH.					
European troops, 1918 scale, normal	92·6	124·8	116·2	492	3610
,, ,, ,, less 10%	83·3	112·3	104·6	443	3250
Indian troops, 1918 scale, normal	55·1	120·4	96·1	592	3810
,, ,, ,, less 10%	49·6	108·4	86·5	533	3430
TURKISH PRISONERS.					
Before capture.					
Sept., 1917. (Documentary evidence.)	30·4	82·4	27·5	490	2603
Aug.–Nov., 1918, average 27th Div. (Document.)	—	—	—	—	2606
Aug.–Nov., 1918, 43rd Regt., 1st F. Art. (Document.)	—	—	—	—	2214
After capture.					
(i) *Non-Labour.*					
Apr.–Sept., 1918, average ration issues, actuals.	37·2	90·5	30·7	492	2684
(ii) *Labour.*					
June–Oct., 1918, average ration issues, actuals.	45·6	102·4	33·3	560	3026
Rations, plus canteen stores, Kantara, 1918.	49·6	110·4	41·3	619	3370
EUROPEAN PRISONERS.					
After capture.					
May–Aug., 1918, ration scale ..	54·7	90·3	28·8	351	2069
Nov., 1918, rations plus canteen stores.	89·7	144·3	120·7	458	3589

The British troops, on adequate B.V.P., remained wholly free from pellagra throughout the war. The Turks suffered from an absolute deficiency of B.V.P., both prior to capture and as non-labour prisoners, although their rations conformed to the standards of diet laid down by hygienists before the importance of the B.V.P. factor was recognized. The B.V.P. of the labour diet was so near the hard-labour minimum of 45 grammes that defective cooking or assimilation or excess of work would reduce it to a relative deficiency, unless high B.V.P. extras were purchased in canteens.

Special interest, as regards the incidence among European prisoners of war, centres in the Maadi camp beside the Nile, where 6,000 Turkish and 2,000 German prisoners were in grass huts adjoining each other, the only discoverable difference in conditions being that of diet. A committee of enquiry, appointed in October 1918, investigated the conditions in these camps in November of the same year, because at that time the Turks had

had sixty admissions for pellagra within two months, while the Germans, many of whom had been there for two years, had remained wholly free. Two hundred of the latter were carefully examined by highly experienced experts, who discerned no case of pellagra amongst them. No German case occurred until early in 1919, when two pellagrins were admitted to hospital after the committee of enquiry had dispersed. The crucial point connected with these facts is that in November 1918 the Turks had no means of supplementing their rations ; whereas the Germans received 2s. a day from a neutral consul, and practically the whole of this amount passed through the canteen accounts. No information was available at the time as to whether this sum was continued to be paid, and, if so, whether these two pellagrins spent it on food or transmitted it to their families when opportunities for so doing occurred on the armistice being signed in November 1918, but investigation of the canteen accounts of 30 out of 79 subsequent cases proved that they had not supplemented their rations in this manner. As they lived on their rations, the low calorie value sufficed to reduce the B.V.P. to a marked relative deficiency. One of the difficulties in obtaining precise information as to the incidence amongst German prisoners is due to the fact that the returns did not differentiate " Germans " from " Other Europeans " until 31st December, 1919. The German cases have been cited as evidence against the B.V.P. theory, on the grounds that the Germans were excellently fed prior to capture, and that some cases developed pellagra after having been some time in hospital. But the information regarding the German ration prior to capture was obtained from a German, who may have been influenced by a desire to exaggerate. It was unsupported by document, and suggested an improbably high dietetic standard for troops whose food-shortage was notorious, and who were serving with an army badly fed and with its transport disorganized. At a time when food-shortage reduced the protein ration of British troops to 112 grms. a day, only reliable evidence would justify the belief that some 7,000 Germans serving throughout the Turkish forces, both on the lines of communication and at the front, were all receiving a ration averaging a protein content of 170 grammes. As regards the hospital cases it is noted that 95 per cent. of the German pellagrins had suffered from dysentery or diarrhœa during the preceding two years ; their powers of assimilation, certainly as regards the 60 per cent. of dysenteries, were probably impaired. That two of them suffered from scurvy is sufficient to discount the statement that their diet contained 450 grammes of fresh vegetables daily.

It is evident, therefore, that no other ætiological theory fits the definitely ascertained facts, and that there is ample support for the conclusion that "*Lack of sufficient biological value of protein stands in ætiological relation to pellagra certainly as an exciting factor and possibly as the determining factor.*"

A similar conclusion was reached during an independent investigation of a pellagrous outbreak among Armenian refugees. The following graph, prepared by the committee of enquiry referred to above, shows the relation of this outbreak and its subsidence to the diet of these refugees. Their camp remained throughout on the same isolated site, on barren desert beside the Suez Canal, where the general conditions remained unaltered.

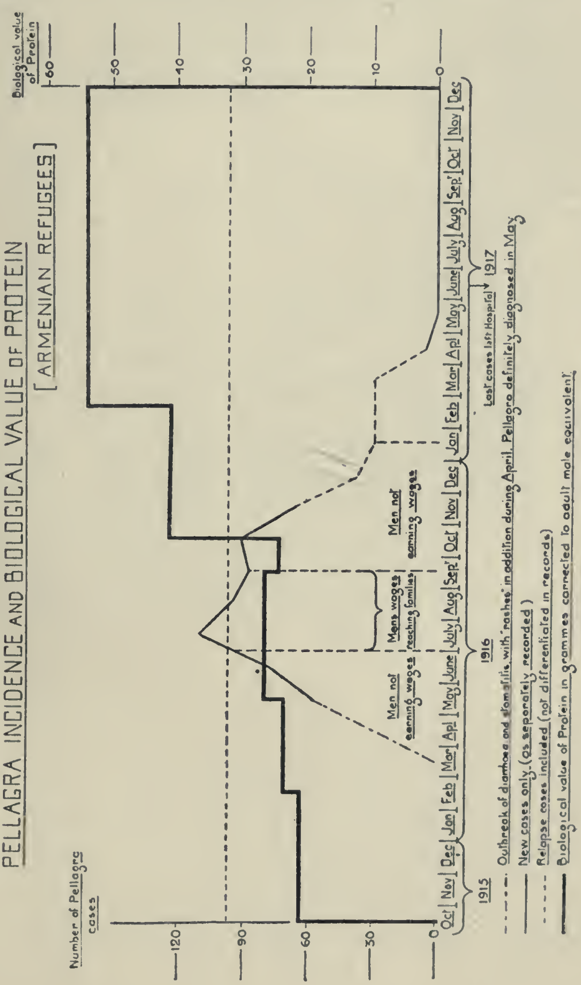


FIG. 3.

The investigation throws light upon the possible mechanism of production of pellagrous symptoms as a result of B.V.P. deficiency.

The ascertained facts were that in the early stages there were hypochlorhydria, loss of protein by lienteric diarrhœa and indicanuria, adrenal atrophy, lowering of the blood-pressure, and degenerative changes in the sympathetic ganglia.

The sequence of the stages between these established changes from knowledge of physiological processes may be regarded according to Professor H. E. Roaf as being as follows :—

Hypochlorhydria, defective protein assimilation, deficient supply of amino-acids (especially tryptophane) to the adrenals or the thyroid, deficient production of adrenalin, lack of this natural stimulus to the sympathetic nervous system, functional failure of sympathetic action, leading to lowering of the blood-pressure and to diarrhœa, degenerative changes in the sympathetic structure, and profound deterioration of the metabolic processes of all tissues in the body.

Establishment of the disease tends to the development of a vicious cycle of malassimilation of protein, putrefactive diarrhœa and rapid evacuation of the lessened amount of protein available for assimilation. Prior to the development and establishment of that cycle and its resultant changes, arrest of symptoms may occur, but experience suggests that there remains some permanent condition, possibly hypochlorhydria, which keeps the pellagrin on the borderland of safety, but liable to relapse at any time if the precarious balance of protein metabolism be disturbed.

There is no special bibliography which deals with pellagra during the war, but a very extensive bibliography is published in a work on Pellagra by Dr. A. F. Harris, of Atalanta, in 1919.

The report of the Committee of Enquiry regarding the prevalence of pellagra among Turkish prisoners of war, was published in Volumes xxxiii and xxxiv of the Journal of the Royal Army Medical Corps.

CHAPTER XXII.

NEPHRITIS.

THE term trench nephritis was applied in 1915 to describe a series of cases of nephritis that occurred in the spring of that year in the British Armies in France and Flanders. In the early months of the campaign, from August 1914 to February 1915, very few cases of renal disease were admitted to hospital, but from March 1915 onwards, and in 1916 and 1917, considerable numbers of cases of nephritis occurred. Inasmuch as the clinical course of the malady was in some respects different from that usually associated with the nephritis of civil life, the term " trench nephritis " was applied to these cases, under the impression that possibly they were of a nature different from other recognized forms. Later, when observation showed that such cases were not restricted in their incidence to men serving in the trenches, the term " trench nephritis " was replaced by that of " war nephritis." This term may be used with propriety if it be held to be descriptive of nephritis as seen under war conditions, but it cannot be regarded as proved that war nephritis is a malady distinct and separate from other forms of nephritis.

Nephritis has not been specially noted by military medical writers in former years, except during the American Civil War. In that war there was a considerable outbreak of the disease, especially in the years 1862 and 1863. The case incidence reached as high a level as 150 per 100,000, and there were in all some 14,000 cases.

In the more recent wars of the last fifty years, acute nephritis does not seem to have been prevalent, and very few cases of renal disease in any form occurred in the British Armies in France and Flanders until February 1915. Prior to this date a few cases of chronic nephritis were seen, especially in reservists who had joined the colours on mobilization, and a very small number of cases of fatal uræmia, sometimes of a very acute type, and associated with the presence of latent chronic nephritis with small contracted white kidneys. Such cases were identical with those seen from time to time in civil practice, where the fatal acute uræmia is the first indication that an extensive chronic lesion is present. It is remarkable that men with chronic lesions of this nature should have been able, as some of them were, to go through the hardships of the campaign during the first three or four months of the war. There was nothing otherwise remarkable in the occurrence of these cases of chronic renal disease, and such cases were seen in small numbers throughout the war; but the number of cases of chronic renal disease that escaped detection and were admitted to the army was very small. This is shown by the results of the examination of the urine in 50,000 men by Captain H. MacLean, R.A.M.C. Casts were found by him to be present in 1·87 per cent., and of these 0·84 per cent. had definite epithelial casts, but doubtless in only a certain proportion of these was serious chronic disease present. In February 1915, a few cases of renal dropsy were observed in the hospitals on the lines of communication for the first time, and in the subsequent months of 1915 the number of such cases increased considerably.

The following table* gives the rates of incidence of nephritis per 100,000 for the years 1915, 1916 and 1917 in France.

Rates of Nephritis and Albuminuria per 100,000 *of strength.*

	1915.	1916.	1917.
January	8·93	69·22	99·27
February	21·08	72·73	100·50
March	34·63	68·49	93·09
April	47·28	54·25	53·01
May	39·63	38·38	51·66
June	55·97	41·60	42·79
July	57·96	39·28	50·51
August	53·02	32·91	49·08
September	41·87	37·86	48·42
October	52·35	61·24	61·30
November	73·98	64·97	63·70
December	72·28	104·40	55·62

The number of cases increased throughout the year 1915, with a slight drop in the months of May and September. In 1915 the highest incidence occurred in November and December, but the rate was also high during June, July and August. In 1916 the highest rates were observed during the winter months, and there was a notable fall from May to September. The rates were especially high from December 1916 to March 1917, but during this period respiratory diseases were very prevalent, especially bronchitis and lobular pneumonia. Nephritis occurred in association with these maladies and not infrequently was a complication of primary respiratory disease. The cases not only swelled the nephritis records, but also greatly increased the mortality rates, and in so far as they were instances of secondary nephritis complicating bronchitis or pneumonia, they really belonged to a different category from that of primary acute nephritis. It is difficult to separate them from primary nephritis in all cases, because in some instances pneumonia occurred as a complication of nephritis, whereas in others the nephritis was a complication of pneumonia.

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* From Report No. 3, dated 7th June, 1918, by a committee appointed in France to investigate war nephritis.

Secondary or complicating nephritis was most often seen in association with respiratory diseases, such as bronchitis, lobular pneumonia and influenza, but other varieties also occurred. Nephritis sometimes occurred in association with cerebro-spinal meningitis, sometimes as a definite complication in a well-marked and typical case, but in others with a more obscure connection. Thus a small number of cases were seen where the onset of disease was characterized by the presence of nephritis and the absence of obvious meningeal symptoms, so that the case seemed at first to be one of ordinary nephritis; yet after the lapse of a variable time, usually a few days, sometimes as long as a fortnight, meningeal symptoms developed, and the case then followed the course usual in cerebro-spinal meningitis. Nephritis of a severe type, and often hæmorrhagic, was not an uncommon complication of infected wounds. These forms of secondary nephritis, with the exception mentioned above, where the disease occurred in association with respiratory affections, are not included in the rates of incidence of nephritis in the army.

Ætiology.

The causation of nephritis is obscure and not as yet certainly determined. Two factors are usually held to be of considerable importance in the ætiology of any given case of nephritis: firstly, the presence of chronic renal disease, and secondly, the occurrence of some acute infection prior to the onset of nephritis, or a history of a previous attack of nephritis that has completely cleared up. It is well known that it is often difficult, if not impossible, to distinguish clinically between primary acute nephritis and an acute exacerbation of chronic or latent renal disease. In several instances in 1915, where a clinical diagnosis of acute nephritis had been made, post-mortem examination revealed that the lesion was really an exacerbation of an old and chronic lesion. Further, many writers have suggested that albuminuria due to trivial causes, *e.g.* functional albuminuria, might predispose to nephritis and be an important factor in its production. The experience gained in the war at any rate throws light on these questions, and affords distinct evidence that these factors were not operative in the great bulk of the cases of acute nephritis. MacLean's observations on 50,000 healthy soldiers showed that in about 5 per cent. some degree of albuminuria was present, and that in less than 2 per cent. casts of some kind were visible. In 0·84 per cent. definite epithelial casts were present, and in 1·03 per cent. only hyaline casts were found. MacLean is of opinion that the army on active service contained at least 1·1 per cent. of men whose kidneys were inefficient and were suffering from some degree of disease, and " that not more than 2 per cent. of the men give any definite indication of kidney disease as indicated by the presence of albuminuria and fairly large numbers of casts." He had the opportunity of observing the influence of this albuminuria on the ætiology of nephritis, as nephritis developed in 161 men whose urine had been examined by him prior to their admission to hospital as cases of nephritis. Of these 161 cases, only 28 had shown albuminuria when examined before going into the trenches, while in the remaining 133 cases the urine had been found to be free from protein. It is therefore evident that, in the great majority of cases, nephritis occurred in men whose urine was known to be free from albumin a short time before the onset of the disease, and that it cannot be regarded as an exacerbation of some previously existing chronic lesion. Although MacLean's observations show conclusively that the great majority of cases of nephritis occurred in men free from renal disease at the moment of onset, there remains the further question as to the proportion of cases that occurred in men who had recovered completely from a previous attack. In a series of 571 cases personally investigated by Sir J. Rose Bradford, a distinct history of previous renal disease was elicited in 62 cases, thus in 10·8 per cent. of cases of acute primary nephritis the patients gave a history of having previously suffered from an attack of dropsy similar to that present at the time of examination, or else stated that they had been in hospital or under treatment for " inflammation of the kidneys " or for " Bright's disease." It is probable that a former attack of nephritis had occurred in more than 10·8 per cent., inasmuch as nephritis occurs not uncommonly without its recognition by the patient, especially when dropsy or hæmaturia is absent.

It may be concluded that, in the great majority of the cases of nephritis in the troops, the attack was not due to an exacerbation of a chronic or latent lesion of the kidneys, nor to the previous occurrence of nephritis. Further, the previous existence of albuminuria cannot be regarded as an ætiological factor of importance.

Nephritis is well known as a complication of many infections, and in many instances the initial illness may be of a trivial character. In 278 cases of nephritis a history of a preceding slight illness, such as " severe cold," " diarrhœa," " influenza," or " sore throat " was obtained in 10·4 per cent. It is, however, remarkable that in 30 per cent. of the cases the patients gave a history of or had distinct signs and symptoms of bronchitis at the actual onset or in the early stages of the disease when admitted to hospital. The bronchitis was not of a severe type, and this association with nephritis was seen in the early cases in 1915. This is a point of some importance, as at that date influenza was not prevalent in the armies, and gas had not been used in warfare. The bronchitis was mild in type, caused no anxiety, and was only of interest in its association with the nephritis. In 100 consecutive cases blood examination for the Wassermann reaction gave negative results. This result is rather striking, as in civil practice cases of acute nephritis of specific origin are not very rare.

The disease was more prevalent during the winter months and decreased during the summer, with the exception of the first summer, that of 1915, when the incidence was unduly high in June, July and August. The winter of 1914–1915 was very cold and also very wet, but the outbreak of nephritis did not occur until the spring, and lasted all through the summer. The greatest number of cases of nephritis occurred in the winter of 1916, and was associated with the great prevalence of very serious bronchitis and lobular pneumonia at this period. It is probable that exposure to wet and cold may act as a predisposing cause, and De Wesselow and MacLean have adduced evidence to suggest that infantrymen, who are necessarily much exposed, have contracted the disease after shorter periods of service at the front than other branches of the service. The malady, however, affected large numbers of men in all branches of the service, and was by no means confined to men serving in the trenches. Thus, in 1915, cases occurred in hospital orderlies living in buildings, and men who had never been to the front, but had served continuously on the lines of communication. In the later years of the war facts such as these could not be determined, since the exigencies of the service caused a greater interchange of personnel. In many instances, where men on the lines of communication were affected, there was no undue exposure to climatic conditions. Further, a small number of cases occurred amongst nurses living under very good conditions. In a series of 332 cases seen in 1915, 285 cases occurred in men serving at the front, and 25 cases in men serving on the lines of communication who had never been to the front ; in the remaining 22 the record of service was not sufficiently accurate to be of value.

No evidence has been obtained in favour of the view that nephritis could be attributed to diet, water, or metallic poisoning.

Cases of nephritis occurred in men who had only been one week in France, but the number of instances in which the disease has occurred in men with less than two months' service in the field is small. In a series of 326 cases analysed in 1915, 195 cases occurred in men who had served six months or less in France, and 131 in men who had served from six to twelve months in France.

Although nephritis occurred in all branches of the service, it was remarkable that only a small proportion of officers was affected. Thus, in 1916, only two officers died from nephritis, and there were no deaths from this disease amongst officers in 1917.

The malady was not confined to any particular age. Cases were met with at all ages from 15 to 56 years of age, but the great bulk of cases occurred in men under 35 years of age. In an analysis of 2,297 cases, 68·72 per cent. of the cases occurred in men over 20 years and under 35 years of age, and 28·3 per cent. of the cases occurred in men under 25 years of age. It is thus evident that a very large proportion of the cases occurred in young men, and that it was not a disease limited in its incidence to the older men. Further, the age incidence of the disease was apparently closely similar to that of the age distribution of the army, since Colonel Hume found that, in a body of some 3,000 hospital patients, 68·42 per cent. were between the ages of 20 and 35 years.*

Perhaps the most striking fact in the ætiology of the disease was the immunity of the native Indian troops. Nephritis was practically unknown amongst these troops in 1915 in France. Although large numbers of Indian sick in three large hospitals were under Sir J. Rose Bradford's observation, he saw no case of the disease amongst them. These troops suffered severely from the hardships of the campaign in the winter of 1914–1915, and more especially from maladies due to exposure to wet and cold, such as bronchitis, lobular pneumonia and trench foot. Notwithstanding the severity of the respiratory affections, especially bronchitis and pneumonia, nephritis did not occur. This immunity of the native troops is most difficult of explanation, since the only difference between them and the British troops, putting aside the question of race, is that their diet and clothing were different; yet there is no evidence to support the view that the disease had a dietetic origin in the British troops. On the other hand, the absence of the malady amongst the Indians is undoubtedly an argument against the disease being due to an infection, probable as this is on other grounds, and at the present time no satisfactory explanation of the immunity of the native Indian troops is available. The case of these troops also throws some doubt on the view that nephritis was the result of some respiratory infection, since, as mentioned above, respiratory diseases were prevalent amongst the Indians.

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* See Chap. xxiii, p. 520.

Morbid Anatomy.

With regard to the morbid anatomy, the renal lesions found in fatal cases of war nephritis were essentially similar in character to those described in other varieties of acute nephritis. In early cases there was intense congestion, with some swelling and irregularity of the epithelium of the convoluted tubules, and hæmorrhage in varying amounts was very constantly present in the tubules. In these early cases glomerular changes might be very slight and inconsiderable. In cases fatal at a later stage the tubular lesions were much more marked, and in these the glomeruli showed marked inflammatory changes, hæmorrhage, exudation and proliferation of the glomerular epithelium, together with hyaline degeneration of the vessels of the glomerular tuft. The interstitial tissue was œdematous and infiltrated with lymphocytes and polymorphs. Lipoid infiltration of the epithelium of the tubules was described, and in some cases of more prolonged duration lesions identical with those of the large white kidney were recorded. Although acute lesions in the interstitial tissue were common in the early cases, overgrowth of fibrous tissue has not been observed.

Shaw Dunn has drawn attention to the presence of pulmonary lesions in fatal cases of nephritis, such as loss of the epithelial lining of the bronchi and the presence of a fibrinous exudate, together with the presence of minute thrombi in the pulmonary capillaries. Capillary hæmorrhages were also found in the spleen and brain, and Dunn has suggested that the renal lesion may be the result of capillary embolism. Capillary hæmorrhages in the brain are, however, not uncommon in other varieties of nephritis, especially perhaps when they are fatal as a result of uræmic seizures of an epileptiform type.

Symptoms.

With regard to symptoms, on the whole there was a remarkable uniformity in their character in the great majority of cases ; such differences as were present were more especially related either to the mode of onset of the disease, or to the presence of one or other of the two main clinical types of the malady.

Thus the onset might be gradual and insidious, or else more or less sudden, although when apparently sudden careful enquiry would sometimes elicit the fact that, for a variable time before the appearance of the more urgent symptoms, there had been an indefinite feeling of ill-health of some duration. Clinically, two main types of the disease were recognized; one, the less frequent, where the leading symptoms were the presence of a moderate pyrexia together with hæmaturia, and the other, and much more common form, characterized by the presence of dropsy, in which pyrexia was either absent or very slight in amount. There were also cases where neither hæmaturia nor dropsy were obvious, but in many of these dropsy had been present but very transitory in character, and had disappeared by the time the patient came under observation in hospital. In the hæmaturic cases associated with pyrexia the onset was often sudden, and this might also be the case where dropsy was a leading feature of the illness, but in many of the latter types the onset was more insidious, and although the patient might date his illness from the day on which the swelling was first noticed, enquiry often revealed the presence of other and earlier symptoms.

Cases of the hæmaturic or hæmorrhagic type occurred from 1915 onwards, but they formed only a small proportion of the total number. The onset was usually sudden and characterized by the presence of general aching pains in the limbs and back, often rather severe, together with headache and pyrexia. The fever was usually moderate—101° F. or 102° F.; exceptionally it might be as high as 103° F. Hæmaturia was marked and the urine obviously bloody rather than smoky. The pyrexia and the limb pains presented some analogy to the initial phenomena of trench fever, and it is, therefore, of some interest that instances of this type were seen amongst the first cases of nephritis observed in the early spring of 1915, and similar cases occurred during the following years. The pyrexia usually persisted for only a few days, but recurrences of pyrexia of short duration were not infrequent. In some cases these recurrences were of a peculiar type, in that a sudden rise of temperature of two or three degrees took place, lasting only a few hours and accompanied by a return or increase in the hæmaturia. These rises of temperature, or "spikes," resembled the recurrent "spikes" seen in trench fever, and they also resembled the transitory pyrexia associated with the occurrence of renal embolism. The resemblance to the latter condition was rendered closer by the fact that the pyrexia was accompanied by an increased or recurrent hæmaturia. It is probable that the occurrence of these cases led some observers to associate trench fever with nephritis. Further, both trench fever and nephritis first attracted attention in the spring of 1915, although nephritis was observed somewhat earlier than the time when clinical features of trench fever were recognized. The more detailed study of trench fever has failed to show that this malady is complicated by the occurrence of nephritis, and thus it is probable that these peculiar recurrent pyrexial attacks were really to be associated with the nephritis, and were not dependent upon the presence of trench fever together with nephritis. Dropsy was usually absent in these hæmorrhagic pyrexial cases, and if present was only slight in amount.

In the dropsical type the onset might be either sudden or gradual. If sudden, the most usual initial symptom was shortness of breath, especially on exertion, such as marching, but sometimes nocturnal dyspnœa of an urgent character was the first symptom to attract attention. The frequency and prominence of dyspnœa as a symptom was one of the most characteristic features of so-called war nephritis, and is probably to be explained by the unusual conditions of active service. Dyspnœa, although a well-recognized symptom of renal disease, is not usually the symptom on which the patient lays most stress in describing the onset of the disease in civil life, but it may well be that on active service, where severe exertion and fatigue are so frequent and necessary, other symptoms are overshadowed by the shortness of breath caused by marching with a pack. If this be the true explanation, it is an interesting example of how the classical symptoms of a well-known disease may vary owing to the conditions under which it manifests itself. In many cases dropsy was the first sign of illness to attract the patient's notice, but this is also a well-known phenomenon in the nephritis of civil life. Although most patients in whom dropsy was obvious also suffered from dyspnœa as an early symptom, dyspnœa might be present without dropsy. Headache was also a frequent early symptom, vomiting was often specially prominent. In a very small proportion of cases, the onset of illness was characterized by the occurrence of very severe uræmic seizures, such as epileptiform fits or amaurosis. In many of these cases there was a chronic and latent lesion present, such as contracted white kidney or the acute exacerbation of a chronic lesion, and it is at least doubtful whether such an onset occurred with primary acute nephritis. Such symptoms at the onset always suggest the presence of chronic disease, notwithstanding the fact that the patient has been apparently well up to a short period before the development of the urgent symptoms.

Œdema was a frequent early sign, and not uncommonly was the first definite sign that led to the man's reporting sick. It was often first noticed in the legs, but swelling of the face or of the abdomen and subcutaneous tissue was not infrequent. The occurrence of ascites, usually moderate in amount, was common even in cases where the general œdema was slight. In a few cases the ascitic effusion was very large. At the time when the patient was admitted to hospital ascites was present in a large proportion of the œdematous cases, and in a not inconsiderable number the pleural cavities also contained fluid. Two facts stand out prominently with reference to the œdema. In the first place, although usually present and often quite marked in amount, it was very exceptional to see the extreme anasarca familiar to all in the renal disease of civil hospitals; and, secondly, the anasarca, even when marked in amount, was in the great majority of cases of short duration. This also is in contrast to what is usually seen in civil practice. In a very large proportion of cases, perhaps in half the cases, the anasarca disappeared in from one to two weeks, and many more cleared up after the lapse of one to two weeks more. This rapid subsidence of the dropsy occurred in cases where it was considerable in amount and was not limited to the slighter and less severe cases. In these slighter cases it was not uncommon for the dropsy to be present only for a few days; many cases were seen where it had disappeared before the patient was admitted to a hospital on the lines of communication, that is to say, where its duration had not been more than three or four days. In a very small number of cases the anasarca was as severe and persistent as that seen in cases of chronic parenchymatous nephritis. Occasionally cases were seen where the patient gave a history of having suffered from a slight transitory dropsy without being sufficiently ill to seek hospital treatment, and then, whilst remaining on duty, the dropsy had recurred to a greater degree and the nephritis had become obvious. Anasarca was not always an initial manifestation; thus in some cases of the hæmorrhagic febrile type, where dropsy was absent at the onset, it supervened later and ran the ordinary course, and dropsy also supervened in many of the cases of gradual and insidious onset.

In a considerable proportion of cases the onset of the disease was gradual and characterized by a general failure of health, together with shortness of breath on exertion, lassitude, backache, loss of appetite, and headache. Many of these men also complained of having suffered from epistaxis. Such symptoms might persist for some days, or even weeks, and then the urine was noticed to be bloody, or dropsy supervened in the legs or face. Shortness of breath was a prominent symptom both in the cases of sudden and in those of gradual onset. It was frequently accompanied by cough, which was usually dry, but sometimes a watery mucoid sputum was expectorated in scanty amount. It was remarkable that the shortness of breath, cough and such pulmonary signs as crepitations were not accompanied by any profuse expectoration. The dyspnœa was not only a very constant early symptom, but sometimes it was of a rather severe type, necessitating an upright posture, and often causing considerable distress at night. In a few cases severe dyspnœa of the type seen in the most severe and fatal forms of uræmia occurred, but one of the main clinical features of all the cases of nephritis, even when not very severe and where ultimate recovery took place, was the frequency of the presence of dyspnœa of a moderate degree of severity.

Vomiting, although not a frequent symptom at the onset, was not infrequent in the subsequent progress of the more serious cases, and diarrhœa was also sometimes observed.

At the onset, and more especially in the numerous cases where dropsy occurred, the quantity of urine was considerably diminished, and the total quantity secreted in the twenty-four hours might be less than twenty ounces. In a few cases temporary suppression, partial or complete, occurred at the onset for short periods of twenty-four hours. No case of death from suppression came under the observation of Bradford. During the onset and persistence of the dropsy the quantity of urine usually remained low, but the subsidence of the dropsy was accompanied by very considerable diuresis. This diuresis was often of abrupt or sudden onset, and was frequently noticed before there was any marked alteration in the degree of dropsy. The increase in the quantity of urine was often very considerable, and quantities of one hundred and fifty ounces might be passed in twenty-four hours. The diuresis, like the subsidence of the dropsy, was prone to occur in the first two weeks of the illness and was, of course, accompanied by a considerable loss in weight of the patient. It might also be accompanied by marked sweating, and, speaking generally, it may be said that sweating was more common and could be induced more readily in these acute cases of war nephritis than is usually the case in the nephritis of civil hospitals. In the latter class of cases the skin is not only abnormally dry, but it is often extremely difficult to cause sweating by any means.

In the hæmorrhagic type, blood corpuscles were present in the urine in abundance, and blood and granular casts were also present. In the anasarcous cases, blood corpuscles could usually be found on microscopic examination. In the slighter cases, where dropsy was absent, blood corpuscles might be absent so long as the patient was kept in bed, but even in cases where the albuminuria had almost cleared up it was remarkable how readily blood reappeared in the urine if the patient was allowed to get up. Casts, hyaline, granular and epithelial, were present in all acute cases, and it was not uncommon for hyaline casts to be present in large numbers. In cases of short duration, where the dropsy and albuminuria cleared up rapidly, the casts also disappeared quickly, and in such cases, where only a small quantity of albumin was present, hyaline casts were only found in very scanty numbers and with difficulty. The centrifugalized deposit contained, in addition to casts, white blood corpuscles, renal cells, and cells from the lower renal tract. Mononuclear leucocytes were present in 36 per cent. of the cases observed by Captain J. A. Wilson. In fourteen cases out of a consecutive series of 100 cases examined by him, organisms were found in catheter specimens of the urine; in three instances *Streptococcus fæcalis*, in three *Streptococcus pyogenes*, in other instances the *B. pneumoniæ*, *B. acidi lactici*, and *Proteus vulgaris*. Twelve of the fourteen cases were of the hæmorrhagic type, but the urine contained no pus, and, although the organisms were virulent, Wilson regarded them as saprophytes and in no way related to the renal lesion. Calcium oxalate and uric acid crystals have been occasionally observed in the urinary deposits.

Albuminuria varied greatly in amount, but in severe cases it was considerable and the coagulum formed on boiling settled on standing to a volume of from one-quarter to two-thirds of the urine volume. In some exceptional instances the urine became solid on boiling; in the less severe cases the amount was less, and even in cases where appreciable dropsy was present the amount of albumin present might still be small. Many cases came under observation after the subsidence of the dropsy, when this had only been present for a few days at the onset of illness, and such cases only showed a slight degree of albuminuria. The albuminuria was more persistent than the dropsy, and was prone to last for several weeks even when the dropsy only lasted for a fortnight or less. It was also liable to increase again when it had begun to subside if the patient were allowed to get up and undergo even mild exertion. Nevertheless, a very considerable proportion of the cases were evacuated to England with only the merest trace of albumin in the urine; in other words, the nephritis, with the resultant albuminuria, cleared up with considerable rapidity. In some cases the albuminuria persisted in the manner so common in many varieties of nephritis of civil life, but this was decidedly exceptional.

Symptoms referable to the vascular system, such as palpitation with some præcordial distress, were not uncommon in established cases of moderate severity, and tachycardia was fairly often seen. Headache, often associated with a heightened arterial tension, was also common and sometimes very severe Not infrequently it was of an intermittent or even paroxysmal type, and an intense headache, with or without an increase in the blood pressure, sometimes heralded the onset of uræmic fits. The blood pressure was raised in the great majority of cases and in the dropsical cases the onset and increase in the dropsy was probably invariably associated with a rise of blood pressure. The rise of pressure was usually moderate and readings above 180 mm. of mercury were exceptional, the usual height being between 140 mm. and 180 mm. of mercury as systolic pressures, and from 70 mm. to 110 mm. as diastolic pressures. Diurnal variations in the blood pressure were common and the evening pressure was the higher. In some cases the difference might amount to as much as 40 mm. of mercury. As the malady progressed towards convalescence the blood pressure fell to the normal, or even below it, and this fall might take place either suddenly or gradually. The fall in blood pressure occurred at the time that diuresis set in with subsidence of the dropsy, and when the pressure reached and remained at the normal height, the diuresis and subsidence of the dropsy were usually completed. In exceptional instances, the blood pressure might fall to a low level before the dropsy had completely disappeared, and in others a high blood pressure might persist notwithstanding the fact that all dropsy had cleared up. In some cases a persistent high blood pressure indicated, as is well known, the presence of chronic disease, but this could not be regarded as certain if based only on the presence of increased tension, since all observers were agreed that one of the most constant phenomena seen in these cases of acute nephritis was a very considerable increase in the height of the blood pressure, and that such rise occurred quite early in the course of the disease. This is quite in harmony with what has been described in former studies of nephritis in civil life.

De Wesselow and MacLean's observations show that a considerable degree of hydræmia was present in the cases of acute nephritis, and that this hydræmia was closely related to the increased tension and usually was also in direct relationship to the degree of dropsy present. In some cases, however, anasarca occurred with little or no hydræmia, and in others considerable hydræmia might be present with but little anasarca. Exceptionally, a high blood pressure might exist without any evidence of the presence of hydræmia.

Although a heightened tension and hydræmia were such constant occurrences, the heart did not in the majority of cases show definite signs of enlargement, but in a considerable minority the apex beat was either in the nipple line or external to it, and returned to a position internal to it on the subsidence of the dropsy and after the fall in the blood pressure. In many of the cases cardiac symptoms, such as palpitation, præcordial distress and inability to sleep on the left side, were present. In some cases the enlargement of the heart was persistent, and was in certain instances dependent upon the presence of chronic renal disease, but this was excluded in the cases where it was temporary in character, and its subsidence coincided with the return to health. The cardiac impulse was usually vigorous and the first sound of the heart was often louder than normal and of a rumbling character.

Anæmia was not a conspicuous feature of the disease except in the rarer instances where the illness was prolonged and of a type similar to that of chronic parenchymatous nephritis, and even in cases where dropsy was very marked it was uncommon to see the pale and waxy facies which is typical of renal disease. Ascites and hydrothorax have already been mentioned as frequent ; pulmonary œdema in varying degrees was also not uncommon and in some cases with uræmic symptoms was very marked. Occasionally the pulmonary œdema was exceptionally well marked at the apices of the lungs, and the abundant crepitations present in such cases sometimes produced signs liable to be mistaken and regarded as pneumonic in origin. It is possible that some of the signs seen in early cases where dyspnœa was a marked symptom were more correctly to be attributed to œdema than to bronchitis.

Inflammatory complications such as pericarditis, pleurisy and peritonitis were quite exceptional, but some of the more severe cases developed inflammatory pulmonary complications, more especially lobular pneumonia and bronchitis.

In striking contrast to the comparative rarity of inflammatory complications, the frequency of uræmic phenomena was a feature of interest, and it is remarkable, when the protean nature of uræmic attacks is taken into consideration, that the very great majority of the uræmic seizures were of the epileptiform type. Other manifestations of acute uræmia, such as coma, mania, urgent dyspnœa or air hunger, were quite exceptional, and when they occurred the case was not infrequently one of an acute exacerbation of a chronic or even of a congenital lesion, such as hydronephrosis, rather than a true case of primary acute nephritis. The epileptiform attacks were generally quite sudden in their onset, and frequently occurred in cases where the general condition was good, and not likely to suggest the probability of such an attack. They might be heralded by the presence of severe headache, and sometimes, but by no means always, were associated not only with a markedly raised tension but also with a sudden increase in such tension. In other cases a general feeling of vague malaise preceded the attack. The fits were generally of a severe type and often a series of them occurred. Notwithstanding their frequency and severity, they were very rarely fatal, either directly or indirectly, and generally the patient recovered completely. Such attacks, even of a severe character, were not limited to serious cases, and although in most cases the urinary flow was scanty at the time of the seizure, such attacks occurred in men passing quantities of urine equal to, or greater than, the normal. Subacute chronic uræmic manifestations were rare and were seen more especially in the exceptionally severe cases that ran the prolonged course of the large white kidney. Analysis of the blood showed that in some of these cases of acute uræmia very large quantities of urea might be present, but, on the other hand, in some instances of severe epileptiform seizures the urea content of the blood was not above the normal.

The examination of the urine in cases of acute nephritis showed that the excretion of urea was not materially affected in the majority of cases, the diminution in the output of the earlier stages being followed by a notable increase during the diuresis accompanying the subsidence of the dropsy. The excretion of chlorides was often diminished, but here also the kidney rapidly regained its power of excretion in the large number of cases that progressed favourably.

Changes in the fundus oculi were rare in the early stages of the malady, but retinitis similar to that seen in chronic renal disease was found in cases running a protracted course. Retinal hæmorrhage was, however, rare.

The review of the clinical course of the disease shows that it is essentially similar to that familiar in civil life, but there are some minor differences. Thus the frequency of dyspnœa as an early symptom is striking, and the very transitory duration of quite serious anasarca is another feature that attracts notice. Further, the severity, frequency and character of the uræmic seizures are peculiar. Such differences, however, do not render it necessary to regard the malady as a new one, or one different from other forms of nephritis. Cases have been seen not only under conditions quite different from those of civil life, but also in very large numbers, and at a very early stage in the evolution of the malady, owing to the exigencies of military life compelling a man only slightly ill to seek medical treatment. It is, therefore, possible that the war has afforded an opportunity of acquiring a more correct view of acute nephritis, especially in its early stages, and that the classical picture hitherto described is more applicable to the more severe forms and the later stages of the disease. Such differences as exist in the clinical course of war nephritis, when contrasted with the nephritis of civil life, may therefore be attributable either to the fact that the man was exposed to fatigue and strain at the onset of the disease, or else to the fact that large numbers of cases were seen at a very early stage of the malady.

Prognosis.

On the question of prognosis, the mortality during the acute stage of the disease was very low ; thus in a series of cases observed in 1915, it was only 0·4 per cent., and the average annual mortality rate for all cases in 1916 was 0·93 per cent., and 1·32 per cent. in 1917. In both of these years the mortality rate was raised by the inclusion of cases of secondary nephritis that occurred as a complication of serious cases of bronchitis and of lobular pneumonia. Further, in some cases diagnosed as acute nephritis post-mortem examination revealed the fact that the malady present was really an acute exacerbation of a chronic lesion, or the occurrence even of acute nephritis complicating a congenital anomaly of development of the kidneys. The great majority of the cases cleared up in a short time, that is to say, in a few weeks, but a residual albuminuria might persist somewhat longer and such cases might relapse if they returned to duty prematurely. A small proportion did not improve and the albuminuria remained with or without dropsy, while some of them ran a course similar to that of the large white kidney, and might be ultimately fatal after the lapse of weeks or months of illness.

Hunter gives the following table for the twelve months, 1st October, 1916, to 30th September, 1917.

Number of nephritis cases admitted to six central hospitals in England		981
Number discharged		741
(*a*) To duty or employments	234=31·5%	
(*b*) To military convalescent hospitals	143=19·2%	
(*c*) To command depots	229=30·9%	
(*d*) Invalided	120=16·2%	
(*e*) Died	15= 2·0%	
Transferred to other hospitals		50
Remaining in hospital or command depot		190

Abercrombie had 171 cases under his personal care in France between April 1915 and February 1916. The results are as follows :—

Discharged		171
(*a*) Showing no further history of nephritis	109=63·7%	
(*b*) Invalided	54=31·5%	
(*c*) Variously accounted for ..	2= 1·3%	
(*d*) Died	6= 3·5%	

Dyke in 49 cases, followed up for various periods under 12 months from the attack, found that 29 or 60 per cent. recovered and were discharged to command depots or to convalescent hospitals; and, of the remainder, five were discharged to employment classified as C3, and 15 were invalided as chronic cases. He also found that the prognosis became worse as age advanced.

It is desirable that the after history of a group of cases should be followed up for a number of years, as the development of chronic nephritis or granular kidney is too insidious to allow any accounts drawn up at the present time to be accepted as final. Still the presumption is that such cases are exceptional. Albuminuria even if profuse might ultimately disappear even after having been present for many months. Patients who had completely recovered so that all albuminuria had disappeared might, however, suffer from second or recurrent attacks especially when exposed to the vicissitudes of military life; hence in all cases even of complete and rapid recovery a prolonged period of some months should precede the return to the conditions of active service No man should be considered fit for full duty whose urine contains albumin and casts when it is known that these are results of a recent attack of nephritis. The question of permanent disability must be answered by a consideration of the condition of the urine, the presence of casts and albumin in reference to the period that has elapsed since the original attack, and the condition of the cardio-vascular system.

Number of Days under Treatment in Cases of Nephritis.

Force from which derived.	No. of Cases.	Total No. of days under treatment.	Average No. of days under treatment.
France	1,928	214,942	111·5
Salonika	9	1,995	221·6
Egypt	35	1,637	46·8
Mesopotamia	7	630	90
Italy	21	3,058	145·6
Total	2,000	222,262	111·1

The foregoing table comprises a series of 2,000 cases of nephritis, taken from the records of patients treated in military hospitals in France, Salonika, Egypt, Mesopotamia and Italy, compiled by the Medical Research Council. It shows the number of days during which patients suffering from nephritis were under treatment.

Diagnosis.

Diagnosis does not as a rule present any very serious difficulties with the exception that sometimes it is difficult to differentiate between a case of primary nephritis and the occurrence of nephritis complicating an old and chronic lesion. The mistake commonly arises from the assumption that the sudden onset of symptoms necessarily indicates the occurrence of a primary lesion, but renal disease in some of its most chronic and insidious forms may exist for long periods without obvious impairment of health, and then quite suddenly urgent and often fatal symptoms rapidly develop. Such cases can often be recognized owing to the presence of signs of cardiovascular lesions such as well-marked cardiac hypertrophy and high tension associated with arterial degeneration. The cases of secondary nephritis complicating acute pulmonary lesions or septic wounds must be carefully distinguished from the primary cases. In military medicine it is also necessary to bear in mind that such a serious disease as cerebro-spinal meningitis may have an onset with nephritis, and the meningeal symptoms, if present, may be erroneously attributed to the supposed presence of uræmia. In all cases of doubt, lumbar puncture should be practised without delay.

Treatment.

The treatment calls for no special notice since it is similar to that usually employed in this disease. During the early stages, when hæmaturia is present or dropsy increasing, the diet should be greatly restricted, and milk is most suitable, but a milk diet should not be continued for prolonged periods merely on the ground of the presence of albuminuria. When dropsy is increasing, some restriction of the fluids is advisable, and many such cases do better on a vegetable or fruit diet than on one consisting solely of milk. It is also advisable, if possible, to restrict the taking of salt in such cases.

Moderate purgation, especially with salines, is useful, and sweating should be encouraged by the use of hot-air baths. Very good results were obtained by the use of improvised lamp baths made with 25-candle power electric lights fixed on an ordinary cradle and covered with blankets. Venesection is of value in the treatment of the uræmic seizures, and sometimes, if practised in the prodromal stage when the tension is high and headache severe, will apparently prevent the occurrence of the seizures. After the subsidence of the dropsy the diet should be increased and should not be restricted merely because some albuminuria is present. Diuretics are of very uncertain value, but sometimes caffein, digitalis or theocin are of service in starting diuresis, and so leading to the subsidence of dropsy. Caffein should only be given for short periods of two or three days, and discontinued unless it promptly produces diuresis, otherwise it is apt to cause vomiting. Tonics should be given during convalescence, especially iron and arsenic.

The patients must at all times be protected against exposure to cold, because chilling may induce a relapse or convert a favourable case into one of the chronic type. This precaution is very necessary during long journeys by rail transport.

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CHAPTER XXIII.

DISORDERS OF THE CARDIO-VASCULAR SYSTEM.

THE functional affections of the heart from which soldiers suffer, known as disordered action of the heart, are of very great importance from a military point of view. They had already been studied by several observers, but recent advances in the knowledge of heart disease have enabled the immense material provided by the war to be utilized more fruitfully than was possible before. The discoveries of Mackenzie, of Lewis, and of others, had impressed upon physicians the importance of observing this great problem from new standpoints, and by new methods, and the large number of the soldiers affected rendered it imperative that every possible facility should be given for their treatment. The results thus obtained may be said to have placed the whole subject on a completely different footing, and to have produced a standard of knowledge higher than was previously attained.

From the earliest days of the war it was evident that cardio-vascular disorders would form a large group of medical disabilities and would present special points of difficulty. After the retreat from Mons many men of the original expeditionary force were sent to England suffering from exhaustion after a period of exceptional physical exertion and little or no sleep. Amongst these weary men were many who complained of pain in the chest, shortness of breath and palpitation on exertion, and were discovered to have a persistent tachycardia. These patients early presented difficulties in treatment and prognosis.

Difficulties also began to arise in the interpretation of certain physical signs. During the first rush of recruiting apparently healthy men were discovered to have abnormal heart sounds and irregularities which threw doubt on their physical fitness. Again, some who had been passed as physically fit broke down early in training with various complaints referable to the cardio-vascular system. Sir James Mackenzie was one of the first to realise that the interpretation of various murmurs heard over the heart during examination of recruits would give rise to uncertainty of diagnosis, and he published a memorandum on this subject. So impressed was he with the difficulties which he foresaw that he drew up a scheme requiring that doubtful cases should be examined by those who had given special attention to this subject. At this time, however, the authorities were unable to adopt Mackenzie's scheme. The question soon became more and more urgent, as hospitals throughout the country were receiving large numbers of recruits or of soldiers back from France who complained of pains in the chest, shortness of breath, palpitation and giddiness on exertion, but in whom no organic disease of the heart could be found. The War Office and the Medical Research Committee consequently arranged for the special study of such cases at the Hampstead Hospital in London, where Dr. Thomas Lewis at first worked in co-operation with an Advisory Committee. Later this work was moved to the military hospital, Sobraon Barracks, Colchester. A large amount of valuable information was soon forthcoming from the studies made by Dr. Lewis and his colleagues at these two hospitals. It was soon realized that the hospital at Colchester could not possibly deal with the large number of cases which arose in England and with those which came from overseas, and in 1918 heart centres were established in the various home commands.

In France it had been early realized that men were being sent over to England with a diagnosis of valvular disease of the heart in whom this diagnosis was not justified, and that a very much larger number was being sent home who complained of trivial symptoms referable to the heart. In 1916 at one base in France an effort was made to collect all cases sent down the line with a diagnosis of valvular disease of the heart (V.D.H.) or disordered action of the heart (D.A.H.) into one centre, where such cases could be sorted and as many as possible saved to France. In 1917 similar centres were started in four other bases, and by this method 50 to 60 per cent. of such cases were kept in the country, a huge majority of whom were previously being sent over to England. These centres continued their work up to the time of the armistice. In certain other war areas a similar effort was made to segregate and sort the various types of cardio-vascular diseases.

Both the medical service and the army were greatly aided by the ultimate development of this organization of centres with specially skilled medical officers in charge of the " heart " cases. The cases in hospital were quickly sorted, and those, in whom real organic disease made full recovery and return to duty impossible, were without delay recommended for discharge from the army.

Still more important was the early return of mild cases to duty together with the skilled medical control of mild cases, so that they should not be overstrained by too early return to work. The network spread by five heart centres at the chief hospital bases in France caught in its meshes a large proportion of the cases of disordered action of the heart, and 50 to 60 per cent. of these were detained for duty in France. Transport to England, loss of time by unduly long stay in hospital there, and the softening of the soldier under home conditions were all saved in respect of about 15,000 men retained in France by this organization. The economy of man-power might have been larger still if the instructions, directing that all D.A.H. cases should be sent to the heart centres and not evacuated to England, had been strictly carried out. But the principles of diagnosis and treatment of these heart cases were only slowly acquired by the medical services in general, and even when the organization of special centres in France and in England had been achieved, there still remained a hesitation to make full use of them.

The total number of cardio-vascular cases dealt with at the several centres in France was very large. From March 1917 to November 1918, over 23,000 cases passed through the various centres. Up to May 1918, 36,569 men had been discharged from the army and the navy for cardio-vascular disorders; and Lewis estimates that at least 70,000 men must have reported sick, but there is little doubt that the true figure is much in excess of this calculation. Since the war it is estimated that one out of every 10 pensioners suffers from some cardio-vascular disorder.

The magnitude of these figures has to be considered in relation to the large number of men engaged in the war. Probably the same percentage of men engaged in previous wars had suffered similarly and Da Costa gave an account of the cardio-vascular disorders of soldiers who had fought in the American Civil War. Da Costa analysed 300 cases and his description embraces nearly all the clinical features of the so-called "soldier's heart" as known to-day.

Amongst recruits and young soldiers in training, cases of soldier's heart, irritable heart, and so on, had frequently been met with. From 1864 to 1868 a committee sat, under the chairmanship of Earl de Grey, to enquire into the condition of soldier's heart in the British Army. It was said to be due to the nature of the accoutrements which the soldiers had to carry at that time and certain alterations were made in them. From 1876 to 1896 various authors ascribed the condition in the British Army to the setting-up drill then in vogue.

With regard to the classification of cardio-vascular disorders, he official nomenclature of diseases includes the terms valvular disease of the heart (V.D.H.) and disordered action of the heart (D.A.H.). There can be no objection to the first title if the diagnosis is correct. Against the application of the term " disordered action of the heart," to the type of case which was so common during the war, much criticism has been directed. The patients who were labelled with this diagnosis were found to be suffering from various diseases in which cardiac symptoms were secondary manifestations or were sequelæ only. It has been frequently stated that the title D.A.H. gives too much importance to the cardiac manifestations, draws the patient's attention to his heart, and induces in every man labelled V.D.H. or D.A.H. the firm belief that he has heart disease. He naturally makes no discrimination between V.D.H. and D.A.H., and the mere diagnosis of " heart disease " suggests to his mind either early death or a crippled future.

The evil results of such diagnosis on the mentality of the patients have, however, been exaggerated. When a man feels his heart beating rapidly, is short of breath and feels pain in the area of his body where he knows his heart resides, he naturally considers that the heart is amiss. Whatever diagnosis is placed on his labels and papers, his mind will be chiefly focussed on his heart because he knows that his symptoms can only arise from some unusual action of his heart. The man's sensations will always be more important to him than the technical diagnosis that he may read on his papers.

But it was early recognized that many underlying causes were responsible for causing shortness of breath, pain in the chest and palpitation, in soldiers, and that one disadvantage of the title D.A.H. was to give too much importance to the cardiac aspect of whatever illness or disability was responsible in each case. Lewis suggested the term " effort syndrome," as the symptoms were chiefly produced on exertion. Though the paramount importance of exertion is true for most cases, in some instances the symptoms occurred chiefly on emotional excitement, and in others they were most distressing at rest in bed. The ideal diagnosis of this type of case would be that of the primary disease. At the present moment knowledge of the condition is not sufficiently advanced to enable such a diagnosis to be made in all cases. The symptoms in most cases can be attributed to an inherent physical defect, an infection, a nervous defect, or to injury to the lung by poison gases. Even though many cases can be thus roughly classified there will still remain many for whom some indefinite diagnosis is necessary, and for whom the title " effort syndrome " is probably more appropriate than disordered action of the heart.

The cardio-vascular disorders met with during the war can then be most conveniently divided into two main types (1) organic or valvular disease of the heart, (2) the functional condition known as soldier's heart, irritable heart or the effort syndrome.

ORGANIC DISEASE.

Certain figures are available which show the number of cases of valvular disease of the heart, among those patients who complained of symptoms indicating a failure on the part of the cardio-vascular system to respond to effort. Amongst 1,000 men in France who went sick with such complaints, only 55 could be shown to be suffering from valvular disease. The following table shows the varieties of valvular disease encountered and the incidence or otherwise of a previous history of rheumatic fever :—

	Number of Cases.	Previous Rheumatic Fever.
Aortic regurgitation	11	6
Mitral stenosis	17	10
Mitral incompetence	19	11
Mitral stenosis and aortic regurgitation	5	4
Paroxysmal tachycardia	3	0
Total	55	31=56·3%

Though 169 cases had been sent down the line with a definite diagnosis of valvular disease of the heart, in only 55 was there any justification for such an opinion. A later series of 7,803 cases from the same base in France showed an even smaller percentage of valvular disease of the heart, viz., 289 or 3·7 per cent. The varieties of valvular disease and the incidence or otherwise of a previous rheumatic fever in these cases are as follows :—

	Number of Cases.	Previous Rheumatic Fever.
Mitral regurgitation	91	53
Mitral stenosis	88	55
Mitral regurgitation and stenosis ..	26	18
Aortic regurgitation	59	24
Aortic regurgitation and mitral stenosis	24	16
Aortic stenosis	1	1
Total	289	167=57·8%

From Lewis' figures of cardio-vascular cases seen in England, which were naturally of a severer type than those examined in France, the percentage of organic disease was about 10.

A subsequent analysis of 500 heart cases examined at a cardiac clinic, in connection with the Ministry of Pensions, shows that the incidence of valvular disease amongst pensioners is considerably higher than that found on active service. The following organic cases were found amongst them :—

Aortic regurgitation	33
Mitral stenosis	16
Aortic regurgitation and mitral stenosis ..	21
Arterio-sclerosis	28
Rheumatic carditis	4
Mitral incompetence	15
Auricular fibrillation (cardio-sclerosis)	6
Total	123=24·6%

The considerably higher incidence of valvular disease of the heart found amongst pensioners than amongst serving soldiers is very striking. Certain explanations seem to account for this. A large number of men who complained of cardiac symptoms on active service probably ceased to attach importance to these symptoms after the armistice or after demobilization. The falling off of cases of functional disease (D.A.H., effort syndrome) would then relatively raise the incidence of organic disease. Medical examiners, realizing the secondary nature of functional cardiac symptoms, may have diagnosed the disability under the heading of the original disease, such as malaria or dysentery.

It had been thought probable that most of the cases of valvular disease of the heart dated their origin from some period before the war, and it was frequently a matter of surprise how well such patients had undergone the physical and mental hardships of active warfare. Acute rheumatic fever was not a common disease amongst soldiers in France, and it is improbable, therefore, that much V.D.H. originated during war service. Yet men with early valvular disease are being seen on pensions boards who have probably contracted the endocardial infection during the war, and since 1918 various observers have remarked upon the greater frequency of infective endocarditis.* This observation is certainly borne out by recent findings amongst pensioners. Both the history and post-mortem examinations make it clear that infection in a large percentage of these cases has invaded the valves of the heart *de novo*, without evidence of previous endocarditis. In other respects the varieties of valvular disease are in no way different from similar lesions met with in civil life.

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* See Chapter vii, p. 197.

Whenever a diagnosis of valvular disease of the heart is made in a young soldier, the patient ought to be discharged from the army. It is unfair to the army and to the soldier to continue his service, both from the risk of further damage and from the fact that the valvular defect has already drawn on the reserve of heart power.

FUNCTIONAL DISORDERS.

The functional disorders of the heart have been described under the terms soldier's heart, irritable heart of soldiers, disordered action of the heart (D.A.H.), and the effort syndrome.

During active warfare various observers found that only 5 to 10 per cent. of those who complained of symptoms referable to the heart could be shown to be suffering from organic disease of the heart. Another 8 to 10 per cent. whose only complaints had reference to the heart were discovered to be suffering from diseases which had little or no relation to the circulatory system. The remaining 80 per cent. complained of shortness of breath, pain in the chest, palpitation and giddiness as their most prominent symptoms. It is to this particular class that special attention has been directed. It has been pointed out above that a large number of men from the expeditionary force and a greater number of recruits at home suffered from these symptoms, and that in these patients no organic disease of the heart could be found. It was soon realized that many different conditions gave rise to these symptoms.

Symptoms.

In 1,000 cases in France, not suffering from any organic disease of the heart or cardio-vascular system, seven hundred and sixty-eight, or 76·8 per cent., complained of pain in the region of the heart. The position and character of the pain varied considerably. The pain was more frequently limited to the region of the apex and to an area extending to a hand's breadth below the apex than to any other part of the left chest. At times the pain was localized in the region of the third left interspace, and occasionally it radiated from one spot in the region of the heart to a wide area on the left side, sometimes also extending to the right side of the chest. Rarely, the pain radiated down the left arm and less frequently down both arms. The character of the pain was most frequently described as a sharp stabbing pain; sometimes an ache or a feeling of soreness was described and many patients likened it to toothache. The pain hampered the breathing and might be accompanied by a sensation of choking in the throat. After the acute pain had subsided patients complained that a varying area of the chest wall remained sore. A study of the histories showed that the first attack of pain was usually determined by some effort or by some sudden mental disturbance, and that, as further strains—physical and mental—were superadded, the attacks of pain became more frequent and lasted longer until they persisted for two or three hours. Complaint was frequently made that pain in the chest prevented sleep and that lying on the left side was an impossibility. It was ascertained that when pain in the heart followed a mental shock some interval of time frequently elapsed before the pain was felt in the chest, though the heart palpitated from the moment of shock. This seemed to suggest that the pain was the result of the excitability and overaction of the heart. The pain was always intensified by exertion and frequently by emotional disturbances. In the majority of cases the pain was associated with hyperæsthæsia or præcordial tenderness of the chest wall, though at the time of examination this might not be present. Two hundred and sixty-eight, or 26·8 per cent. of the cases, had this tenderness. The examination took place within forty-eight hours of the patients' arrival at the base.

Six hundred and seventy-five, or 67·5 per cent., voluntarily complained of shortness of breath on exertion, though on enquiry the remaining 32·5 per cent. acknowledged that they were short of breath on slight exertion. The majority showed no increased respiratory rate at rest, but they were more breathless than normal individuals after the same amount of exertion. Occasionally, however, even when the patient was at rest, his breathing was rapid and shallow, a type seen in civil life in definite cases of hysteria. In such cases a respiratory rate of 60–80 per minute was frequently counted and a rate of 200 per minute is recorded by Lewis. Sighing respiration was common. It was noteworthy that the pulse rate might be very high (140–150), and the respiratory rate only very slightly increased (24–26).

Four hundred and three, or 40·3 per cent., mentioned giddiness as the chief subject of complaint. It sometimes occurred with exertion, but more frequently on the resumption of the erect posture after sitting or after recumbency. Occasionally it was sufficiently severe to cause the individual to fall, and the vertigo has been sufficient to cause a man to fall from his horse. It was frequently noticed that men were giddy after certain Swedish exercises, particularly on rising to the feet after the completion of leg movements while lying on the back Attacks of palpitation were usually accompanied by sensations of giddiness or fullness of the head.

Not all patients with a rapid heart action were conscious of discomfort. Three hundred and fifty-four, or 35·4 per cent., complained of palpitation, fluttering of the heart and heavy beating of the heart. Complaints of the heart turning over and isolated heart thumps were usually indicative of the occurrence of premature ventricular beats. Palpitation usually occurred in bouts and the rate of the heart during an attack often reached 180 beats per minute. The attacks lasted a variable period from 20 minutes to five or six hours. Many graphic records were taken during attacks of palpitation and these showed in all cases a normal rhythm. Records of paroxysmal tachycardia and auricular fibrillation placed the cases in the categories of organic disease. Ordinary palpitation followed most acutely on exertion or after some emotional disturbance. Frequently patients complained that palpitation prevented sleep. One hundred and twenty-three, or 12·3 per cent. of the cases stated that they were subject to fainting attacks. It was frequently difficult to diagnose the attacks which patients described as faints. Some were undoubtedly syncopal attacks, and Lewis and MacIlwaine have described in detail their observations during such attacks. Their accounts make it clear that the attacks observed were vagal in origin. Many patients stated that giddiness and a failure of vision compelled them to lie down, indicating a pre-syncopal condition. Some, however, who had complained of fainting attacks, were observed to have undoubted hysterical seizures.

In addition to the above there were certain disabilities in most cases, which had less reference to the cardio-vascular system, and were probably directly due to the original disease.

Nearly every patient complained that he was exhausted by degrees of physical exertion which he was previously well able to support. Many had a worn out and fatigued aspect, and while in hospital it was almost impossible to keep them from lying down.

Headache was a common complaint, as also was sleeplessness. Many stated that they had been sleepless for some weeks before they finally broke down. The irritability of temper commonly encountered was an evidence of the general exhaustion of the nervous system.

With regard to the physical signs in these cases, about one-third had tenderness of the left side of the chest wall. The muscles and ribs were tender on pressure and pinching. The tender area varied in size and distribution ; the area which was found to be most commonly affected was that in the neighbourhood of the apex beat. A less common area involved the third and fourth ribs with the intervening interspace. At times the whole of the præcordial area was tender together with the left pectoral muscles and the inner side of the left arm. The degree of tenderness varied from time to time in the same individual, and was a guide to the grade of exercise which the patient ought to undergo. According to Lewis præcordial tenderness seemed to be more frequent in those patients who gave a history of rheumatic fever. It was always considered to be a bad prognostic sign if the tenderness continued throughout a course of treatment by graduated exercises. In eliciting information of any kind from patients of this class it was always important to avoid suggestion. If real tenderness was present the patient would invariably wince if, without any remark to the patient, the ribs and interspaces were pressed upon.

Many observations have been made on the rate of the heart under varying conditions of rest and activity. The average rate of the heart was about 85 per minute in unselected cases. During the waking hours the rate remained quick, but in the majority it appeared to become slower in sleep. In this connection an interesting observation was made by Marris in France on a case of tachycardia following typhoid fever. While taking a continuous polygraphic record he noticed that the rate suddenly halved. On looking at the patient he found that he had fallen asleep. Immediately on awakening the rate returned to its original rapidity. This was corroborated during an enquiry into the cardiac disorders of soldiers in France for the purpose of noting, in a large number of cases, the heart rate when the patient was asleep. It was found to be the almost invariable rule that the rate fell remarkably in this class of cases; for instance, heart rates of 120 or thereabouts, which persisted during the whole of the waking hours, would be counted at 60–70 when the patient slept. Further enquiry in cases of tachycardia in every sort of disease will show the value of this observation. It seems to suggest the preponderating influence of the nervous system in this class of tachycardia.

The following table indicates the pulse rates of the 1,000 cases examined, taken in the erect position, after a rest.

Pulse Rates.

Rate.	Percentage.	Rate.	Percentage.	Rate.	Percentage.
40–50	0·1	80–90	13·5	120–130	11·3
50–60	0·5	90–100	22·4	130–140	1·4
60–70	1·8	100–110	23·8	140–150	0·9
70–80	9·5	110–120	14·7	150–160	0·1

In response to exercise the rate increased to a higher level than in normal individuals, and after slight exertion it was quite common to find the rate increased to 170–180 beats per minute. Further, a longer interval of time elapsed after exertion before the pulse returned to its original rate. In healthy men an increase of 20–30 beats per minute after brisk exercise will disappear and the rate will return to normal in a minute or less. In the D.A.H. type of case it frequently required an interval of more than two or three minutes after the cessation of the exercise before the heart returned to its original rate. Considerable stress is laid on this phenomenon at the examinations by pensions boards. Most patients in whom there is a tardy return to the pre-exercise heart rate show considerable respiratory distress and may complain of pain in the left side after such an exercise as mounting a chair ten times with each leg. As Lewis points out, the pulse rate as a guide to capacity has to be circumspectly used, and in France it was frequently noticed that men who had a persistent pulse rate of 120 could play a hard game of football or go for a march without ill effect.

The two chief types of arrhythmia met with in cases with the effort syndrome are sinus arrhythmia and premature contractions of the ventricles. The discovery of heart block or auricular fibrillation immediately places the case in some category of organic disease. In young people with slowly acting hearts, *e.g.*, 60–70, a degree of sinus arrhythmia is common. The irregularity is complete and is much influenced by the varying phases of inspiration and expiration, the heart usually becoming markedly slower at the beginning of expiration after a deep inspiration. When the heart is quickened by exertion or excitement the arrhythmia disappears.

Frequent premature contractions arising in the ventricles were noted in 5·7 per cent. of the 1,000 cases. These were usually felt as intermissions in the radial pulse but the premature contractions of the ventricles could be heard with the stethoscope. They tend to disappear when the heart rate is quickened. In fact, this characteristic response to effort with disappearance of the irregularity separates the irregularities which are significant of disease of the heart from those which are of no importance. The only common irregularity which is of great importance is auricular fibrillation, and in this type of arrhythmia the irregularity becomes more marked after exertion and the breathing of the patient is usually impaired.

Minor differences in the size of the heart were extremely difficult to detect, and usually the earliest reliable sign of increase was some displacement of the apex beat towards the axilla. The maximum impulse of the heart is often forcible and the powerful thrust against the chest wall gives the impression of hypertrophy. Two facts seem to militate against the view that a forcible impulse at the apex indicates hypertrophy in this class of case; first, the impulse is found at a normal distance from the mid line of the sternum, and secondly, it is only forcible when the heart is beating excitably and becomes much less obvious after the patient has lain in a recumbent position for some time. Careful orthodiagraphic measurements by Meakins and Gunson support the view that the heart is not enlarged, either at rest or immediately after exertion. By careful measurements of the distance of the apex beat from the mid line of the sternum and by percussion, it was never possible to demonstrate any change in the size of the heart while the patient was under observation, though in some the apex beat appeared to be diffuse. In such cases it is necessary to localize the maximum impulse, and it will be found that it lies well within normal limits. Diffusion of the impulse is often found in cases which suffer from palpitation.

A sharp distinction has usually been drawn by all observers between the murmurs which occur in diastole and those which occur during systole of the ventricles, namely that diastolic murmurs invariably indicate an organic lesion. Systolic murmurs were extremely common in the effort syndrome patients, and they were heard in 200 out of 500 cases in which special attention was directed to this point. The significance of systolic murmurs heard over the præcordium has given rise to much discussion and frequently to gross misinterpretation. Many men were refused admission to the army, have been discharged from the army, and have been wrongly assessed by pensions boards, on account of the misinterpretation of a systolic murmur. In the early days of the war, Mackenzie published a brief instruction on this point by direction of the Director-General of the Army Medical Service. He pointed out that an estimate of the fitness of any heart should not be judged by the hearing of a murmur alone, and that in every case the position of the maximum impulse and the response of the heart to effort should be the guiding factors in forming an opinion. Most hearts beating at a rate of 110 or more are prone to generate præcordial systolic murmurs. Many murmurs which have no untoward significance can be detected by their auscultatory characteristics alone. A systolic murmur heard best over the pulmonary cartilage can usually be immediately disregarded; this area has always been referred to as the "romantic area." Systolic murmurs heard best over the aortic cartilage are less common than those heard over the pulmonary cartilage. In men over forty a systolic murmur over the aortic cartilage may indicate loss of elasticity and some dilatation of the aorta without any incompetence of the aortic valves, and without any evidence of hypertrophy of the left ventricle. Systolic murmurs heard best over the aortic cartilage, have, however, a sinister significance when they are associated with a diastolic murmur, usually heard best at the left of the sternum, and with obvious hypertrophy of the heart.

The chief difficulties are met in connection with systolic murmurs heard best in the neighbourhood of the apex beat. Probably the murmurs heard in this locality are generated by varying factors, as for instance the cardio-respiratory murmur which is dependent upon the relationship of the heart to the lung. It may be caused by a normal breath sound being broken into two or three short murmurs, each of which accompanies a cardiac systole ; at times it is accentuated by inspiration and at times by expiration ; it disappears when the breath is held, and pressure with the bell of the stethoscope against the chest wall tends to obliterate it altogether. There are other systolic murmurs heard best in the neighbourhood of the apex, whose characteristics appear to suggest a leak at the mitral or tricuspid orifices. These are blowing murmurs which are conducted towards the axilla and may be heard at the angle of the left scapula. More rarely a high pitched blowing murmur may be heard best toward the lower end of the sternum which has the characteristics of the murmur in a similar position in uncomplicated tricuspid regurgitation. In a case where such murmurs are to be heard no importance should be given to the murmur unless there is some displacement of the apex towards the axilla and unless there is some limitation of the heart's response to effort. In all cases of systolic murmurs about the apex beat particular attention should be paid to the accentuation, or otherwise, of the pulmonary second sound. Whether the tricuspid and mitral valves may be temporarily incompetent in perfectly normal hearts is not known but in all cases no importance should be placed on the mere hearing of a systolic murmur without other evidences of cardiac disability.

With regard to blood pressure, when patients were going about in a convalescent camp in France it was found that the systolic pressure ranged between 130–150 mm. Hg., while Lewis found under conditions of rest the blood pressure was usually more or less normal. Lewis points out that the reaction of the blood pressure to effort was exaggerated in cases of D.A.H. With the same amount of work the systolic pressure rose 48 mm. Hg. in two patients with effort syndrome, while in three controls the average rise was only 19 mm. Hg.

Cold, blue hands and feet were frequently seen and many instances of Raynaud's disease were encountered. Many patients were quite positive in their statement that the circulation of the hands was quite normal before the onset of their other circulatory symptoms. The skin of these patients readily perspired and it was not uncommon to find them becoming bathed in perspiration during examination. The pilomotor and other reflexes of the skin were usually very active.

Blood counts revealed a leucocytosis in many cases.

Physical evidences of excitability of the central nervous system were two in number; first, general tremulousness was common and a fine tremor of the outstretched hands was noticeable in many patients. Secondly, the knee jerks were usually accentuated.

Ætiology.

With regard to the predisposing causes of disordered action of the heart, the symptoms and signs may be due to so many underlying causes that it is necessary to have a detailed history of each man's previous health and occupation and his own account of the factors which seemed to lead to his breakdown. Particular attention must be paid in each case to the date of the onset of the symptoms and it is noteworthy that in 542 out of 1,000 cases the disability had been noticeable before enlistment. The following show the various conditions which were alleged by these patients to be the cause of their disability :—

Cases occurring before Enlistment.

Indefinite gradual onset	in	308	cases, of whom	191	were	discharged fit.
Rheumatic fever	,,	82	,, ,, ,,	40	,,	,, ,,
Definite effort or shock	,,	56	,, ,, ,,	30	,,	,, ,,
Faints and fits	,,	21	,, ,, ,,	12	,,	,, ,,
Pneumonia	,,	18	,, ,, ,,	9	,,	,, ,,
Typhoid fever	,,	14	,, ,, ,,	7	,,	,, ,,
Scarlet fever	,,	9	,, ,, ,,	4	,,	,, ,,
Influenza	,,	9	,, ,, ,,	1	was	,, ,,
Pleurisy	,,	6	,, ,, ,,	6	were	,, ,,
Rheumatism	,,	4	,, ,, ,,	1	was	,, ,,
Diphtheria	,,	3	,, ,, ,,	1	,,	,, ,,
Malaria	,,	3	,, ,, ,,	2	were	,, ,,
Tonsillitis	,,	2	,, ,, ,,	1	was	,, ,,
Asthma	,,	2	,, ,, ,,	1	,,	,, ,,
Jaundice	,,	1	,, ,, ,,	0	were	,, ,,
Other conditions	,,	4	,, ,, ,,	2	,,	,, ,,
Onsets before enlistment	,,	542	,, ,, ,,	308	,,	,, ,,

Of these cases 56 attributed the onset of their symptoms to some definite effort and strain or to some sudden mental excitement and shock. Of the various infectious diseases, rheumatic fever largely predominates, though the patients did not show signs of valvular disease of the heart. As the pathological process in rheumatic fever is the deposit of small inflammatory collections of cells in various parts of the heart muscle and valves, it is quite conceivable that an impaired muscle results from the disease without any deformation of the valves. Four hundred and fifty-eight of the 1,000 cases of D.A.H. analysed occurred after enlistment, and were attributed to :—

Cases occurring after Enlistment.

An indefinite gradual onset	in	238	cases,	of	whom	148	were	discharged	fit.
Definite effort	,,	57	,,	,,	,,	26	,,	,,	,,
Shell shock	,,	36	,,	,,	,,	20	,,	,,	,,
Pyrexia of uncertain origin	,,	31	,,	,,	,,	26	,,	,,	,,
Being buried	,,	21	,,	,,	,,	13	,,	,,	,,
Being gassed	,,	18	,,	,,	,,	8	,,	,,	,,
Wounds	,,	11	,,	,,	,,	6	,,	,,	,,
Trench fever	,,	8	,,	,,	,,	6	,,	,,	,,
Dysentery	,,	8	,,	,,	,,	3	,,	,,	,,
Influenza	,,	6	,,	,,	,,	6	,,	,,	,,
Fits and faints	,,	5	,,	,,	,,	1	was	,,	,,
Bronchitis	,,	4	,,	,,	,,	2	were	,,	,,
Rheumatic fever	,,	3	,,	,,	,,	0	,,	,,	,,
Scarlet fever	,,	2	,,	,,	,,	0	,,	,,	,,
Tonsillitis	,,	2	,,	,,	,,	2	,,	,,	,,
Jaundice	,,	2	,,	,,	,,	1	was	,,	,,
Rheumatism	,,	2	,,	,,	,,	0	were	,,	,,
Measles and pneumonia	,,	2	,,	,,	,,	2	,,	,,	,,
Pleurisy and anæmia	,,	2	,,	,,	,,	2	,,	,,	,,
		458				272			

The patients who were unable to attribute the onset of their symptoms to any definite cause, stated that the exertion of training or the additional strain, both mental and physical, to which they were subjected in France, had gradually told upon them. The other special predisposing factors, peculiar to the conditions of active service in the field, were wounds, being buried or gassed, shell shock and various infections. In the case of the wounded who later complained of cardiac distress, there had usually been a prolonged period of sepsis and rest in bed, and the effects of both on the circulatory system were probably analagous to those following infectious fevers. More and more importance has been given to infection as a cause of effort syndrome, and many of those whose onset was indefinite may have belonged to this category.

Investigations in a convalescent camp in France showed that many cases were still suffering from what was probably trench fever at the time of admission. Lewis gives the following percentages as demonstrating the greater frequency of a history of previous infection in patients suffering from the effort syndrome than in those suffering from various gunshot wounds but with no effort syndrome.

Prevalence of previous diseases in effort syndrome patients observed in 1914–1915, *as compared with patients without effort syndrome.*

Previous Illnesses.	Effort Syndrome (558 Cases observed).	Heart Disease (101 Cases observed).	Gunshot Wounds (100 Cases observed).
No past illness or accident	18%	11%	82%
Rheumatic fever or chorea	23%	61%	4%
Pyrexia of uncertain origin or influenza	12%	6%	0%
Enteric or enteritis	8%	1%	4%
Dysentery	6%	3%	2%
Pneumonia.. ..	6%	10%	3%
Scarlet fever ..	5%	1%	1%
Bronchitis	3%	0%	4%
Tonsillitis	8%	6%	0%
Malaria	3%	0%	6%
Venereal disease ..	2%	4%	5%
Pleurisy	16%	1%	3%
Trench fever ..	5%	0%	0%
Trench foot ..	9%	3%	0%
Other illnesses ..	87%	5%	0%

It has long been recognized with what frequency patients complain of their hearts during convalescence from various infective diseases. In civil practice influenza is one of the commonest of these infections. During the war certain observations on the physical impairment of the circulatory system following typhoid fever and trench fever have been made; in both diseases a persistent tachycardia may arise after the acute phases of the disease have passed away, even before the patient has left his bed. These observations seem to show that such infections upset the nervous control of the heart or impair its musculature before any additional strain, such as the resumption of the erect posture, has been thrown upon the heart. A quick pulse-rate during convalescence from diphtheria, for example, necessitates prolonged recumbency if danger is to be averted.

As regards the age incidence of D.A.H., 56·4 per cent. of 1,000 cases analysed were between 20 and 30 years of age. The majority of men serving in France were probably of this age group, for an analysis of the age groups of 2,000 patients who were not suffering from effort syndrome gave a similar percentage of men between 20 and 30 years of age. The percentages in quinquennial periods are almost identical in both the effort syndrome and other cases as is shown in the following table.

Age.	Percentage 1,000 cases D.A.H.	Percentage 2,000 other cases.
15–20 years	7·9	11·15
20–25 ,, ...	33·3	32·95
25–30 ,, ...	23·1	22·05
30–35 ,, ...	13·8	13·05
35–40 ,, ...	10·9	11·55
40–45 ,, ...	8·4	7·5
Over 45 ,, ...	2·6	1·75
	100·0	100·00

Analyses of cases made by Hume and Lewis seem to indicate that soldiers who eventually suffered from the effort syndrome had been drawn mainly from sedentary or light occupations. This was the case in 64 per cent. of the cases coming to a heart centre in France.

Various incidental inquiries into the influence of other factors in the production of the symptoms of the effort syndrome have been carried out by different observers.

Parkinson and Koefod came to the conclusion that the smoking of a single cigarette raised the blood pressure and increased the frequency of the pulse both in controls and in cases of disordered action of the heart. They also found that the smoking of a few cigarettes rendered healthy men more than usually breathless on exertion, but breathlessness occurred more frequently and more severely in a large proportion of patients with the effort syndrome. They were of opinion that excessive cigarette smoking was not the essential cause in most cases of disordered action of the heart, but that it was an important contributory factor in the breathlessness and præcordial pain of many of them. That the condition is frequent in the Sikh soldier, to whom smoking is forbidden, is a further proof that tobacco does not play a large part in the production of the effort syndrome.

Lewis pointed out that palpable enlargement of the thyroid was only found in 19, or 4 per cent. of 502 soldiers specially examined, amongst whom was one case which showed the associated phenomena of Graves' disease. Further, there is no increased incidence of tachycardia in those soldiers who have a palpable enlargement of the thyroid. That the thyroid gland does not play a part in the causation of the tachycardia in this class of case is further supported by the fact that in D.A.H.

patients the pulse-rate falls markedly in sleep, whereas in exophthalmic goitre the drop in the pulse-rate is never complete.

Of the various gases used by the Germans, phosgene was accountable for more cardiac disabilities than any other. It is probable that far more men were gassed by mustard gas than by phosgene; but those patients who suffered from D.A.H. symptoms shortly after poisoning by mustard gas were almost invariably those who had spent a considerable period in hospital with bronchitis or broncho-pneumonia following the gassing, and in the production of whose symptoms a large element of sepsis entered. The various sternutatory gases never produced circulatory after-effects.

About 8 per cent. of cases dated their disability from mental disturbance following the bursting of a particular shell or as the result of a long-continued intensive bombardment. The impression obtained in the shell-shock centres in France was that tachycardia developed in about 20 per cent. of the cases while the patients were still in bed. Many of those whose disabilities began imperceptibly and gradually, attributed their condition to the wear and tear, mental and physical, of life in the trenches.

With regard to venereal disease as a predisposing cause, the patients were for the most part of an age at which syphilitic conditions in the heart and arteries do not occur. A history of recent infection could be obtained in only 4 per cent. of Lewis's cases. Without any particular inquiry it was certain that very few of the D.A.H. cases in the various centres in France were suffering from gonorrhœa. These men were closely scrutinized, and the routine inspections for scabies and staining of the clothes with discharges sufficed to detect most cases of gonorrhœa.

With regard to alcohol as a predisposing cause, Lewis found that 53 per cent. of effort syndrome cases were total abstainers, as compared with 33 per cent. total abstainers amongst cases of wounds and not suffering from D.A.H. Conscientious reasons were chiefly given for total abstinence and this explanation gains support from the greater refinement and more frequent introspection found in cases suffering from the effort syndrome. They were usually men who took great care of themselves.

In estimating the prime factors which underlie the disability of the effort syndrome, the above evidences of previous history, previous infections, the symptoms of which the patient complains and the signs found on examination have to be taken into consideration. By so doing, most cases can be placed in one of six fairly distinct categories. To illustrate this the following table was compiled from the detailed examination of 375 effort syndrome pensioners seen at a cardiac clinic :—

17	or	4·5%	poor physique.
137	,,	36·6%	previous infections.
110	,,	29·3%	had neurasthenia.
33	,,	8·8%	had been gassed.
24	,,	6·4%	had history of single strain.
15	,,	4·0%	had long service.
39	,,	10·4%	were of doubtful category.
375		100·0%	

With regard to the poor physique group, the men stated that they attempted an apprenticeship to some strenuous occupation, such as shipping and coal mining industries, but that they were compelled to leave such work for a less severe and usually sedentary form of occupation. When such men become soldiers they are called upon to undergo exertion which is beyond their physical powers. In the war many young men of this type might have developed into efficient soldiers by a slow and gradual training, if sufficient time and gradation of training had been possible, but the sudden rush of the civil population into the army precluded this gradual method of development.

In France a careful physical examination was made of some hundreds of patients who passed through the heart centre at Boulogne with a view to their physical comparison with German prisoners, of whom nearly a thousand were similarly examined. The differences in certain directions were extremely marked. The later muscular development around a rickety chest wall may be taken as an example. In a German of poor natural physique, or one who had some acquired deformity such as a rickety chest, the defect was minimized by compulsory service involving exercises in the gymnasium or swimming baths. Youths in Germany had been educated and compelled by their Government to take this form of exercise. The universal provision of gymnasia and swimming baths in towns and villages enabled them to continue their physical training, the value of which they had been taught during compulsory service in the army, and for which the majority had a real liking. On rickety frames the German had often built a good musculature, and at the same time had developed the lung and heart capacity to the maximum. On the other hand, it is probable that only a small percentage of the new armies formed in the United Kingdom during the war had ever played any game or undergone physical training. Interest in games had been to a large extent confined to watching instead of participating in them, and the result showed itself in the poor expansion of the chest and under-development of the general musculature, in which the heart participated. The physical effort necessitated by training and service in the army very soon proved too much, therefore, for individuals with a naturally poor physique.

With regard to the group of cases which had suffered from previous infections, the conditions of active service inevitably cut short the necessary rest—mental and physical—required for complete recovery from the various infectious diseases. In typhoid fever and trench fever a tachycardia may arise towards the end of the illness at a time when the fever has disappeared and while the patient is still in bed. Again, severe infections tend to reduce the systolic blood pressure during the course of the fever. This is invariable in typhoid fever and pneumonia, but is less constant in trench fever. Consequently cardio-vascular symptoms arising after recent attacks of typhoid, trench fever, influenza and pneumonia are usually clearly related to the infections of these diseases. Occasionally, however, the relationship is not so obvious.

Residual abscesses from wounds, causing in themselves little inconvenience, have been found to give rise to an intoxication which produces a clinical picture of D.A.H. Similarly, small collections of pus in deep wounds of the leg, and small septic collections round foreign bodies in the pleural cavity, have been the immediate cause of the more general symptoms of shortness of breath, palpitation and pain in the region of the heart on exertion. The removal of the infection and the opening and draining of the abscess have led to the complete disappearance of the symptoms.

The influence of rheumatic fever in producing D.A.H., quite apart from the production of valvular disease, has also been brought to light by different investigations. It was found that the percentage of D.A.H. cases who had previously suffered from rheumatic fever varied from 11 to 23 per cent. of the cases examined. It must therefore be assumed that the micro-organism of rheumatic fever causes some permanent damage to the muscular fibres of the heart, and this is suggested by the observations of Carey Coombs on the pathology of the disease. He points out that the characteristic feature of this infection is the collection of small subsidiary nodules among the heart muscles and between the bases of the valves.

It is probable that many other infections may be as responsible for the persistence of symptoms of the effort syndrome as those already mentioned, but their relationship has not been so clearly proved. Many soldiers who had gone sick and had come down the line with only D.A.H. symptoms were found to be pyrexial, and it was evident that they had suffered recently from fever. Many had obviously suffered for some time from trench fever. It is possible, too, that mild, indeterminate fevers, such as occur in catarrhs of the upper respiratory passages, might alone bring on the symptoms of the effort syndrome in men tired or strained during active fighting.

In associating the symptoms with any particular fever, the interval of time between the occurrence of the fever and the onset of the symptoms is of considerable importance. In the case of rheumatic fever the infection is known to produce permanent changes in the heart muscle, and a remote history of rheumatic fever is always to be considered as a possible causative factor. In other infections the association in point of time ought to be much closer than in rheumatic fever. But if the patient has passed a period of perfect health and has been well able to sustain exertion between the period of convalescence from the fever and the onset of the symptoms, some other causative factor ought to be sought.

Of the various poison gases, phosgene was the most potent in its effects on the heart. Occasionally soldiers who had been exposed to phosgene gas suddenly dropped dead at varying intervals up to some days after exposure. This usually occurred after exertion and was only partly due to sudden œdema of the lungs; the cause seemed to lie in heart failure. The more remote effects of breathlessness, pain in the chest, palpitation and giddiness occurred in a larger majority of men poisoned by phosgene than of those poisoned by any of the other gases. The after effects of mustard gas seemed to depend rather on the severity and nature of the septic pulmonary complications than on any clinical evidence of direct implication of the heart itself.

The " sneezing " gases, blue cross, never produced any after effects on the lungs or on the heart, and some other cause than gassing must be sought in men who had been exposed to this type of gas alone, and who developed later the symptoms of the effort syndrome.

Various pathological changes in the lungs have been described as the after effects of phosgene and mustard gases. Emphysema and peribronchial fibrosis are two sequelæ to which attention has been drawn by French observers in particular. Such pulmonary changes may interfere with the respiratory exchange of oxygen and carbon dioxide in the alveoli and so produce breathlessness and cardiac distress on exertion.

As regards the effect of sudden exertion and strain, a small percentage of men stated that they felt perfectly well until they were buried and as a result had to struggle and strain every muscle in the body to escape. Added to the physical effort there was in all such cases a severe nervous shock, and it is always difficult to assess the respective value of the physical or the mental strain as the causative factor.

It has been disputed by many whether muscular exertion acting on a healthy heart can ever produce any lasting effect. Those who deny that any physical effort, however severe and however mechanically disadvantageous, can produce any lasting effect on the heart attribute the effort syndrome to the effects of exertion on a damaged heart muscle. According to this view the strain merely determines the failure of a heart damaged by some infection or toxic agent. If this is the case, it is extremely difficult to point to the infective or toxic agent in some cases of this group whose previous history and examination give no evidence of recent or remote infection. Nor can nervous influences play any part, as this type was frequently seen in men working at a base, whose symptoms dated from a merely physical strain such as cranking up a car.. In civil practice healthy boys and young men get similar symptoms after strenuous games, and in industrial life perfectly healthy miners have complained of the same train of symptoms after struggling to get a full tub, which had become derailed, on to the lines again. Many other instances could be quoted, and the balance of clinical evidence is certainly in favour of the view that sudden exertion or prolonged effort may be the starting point of the symptoms of the effort syndrome.

Various phenomena indicative of nervous exhaustion were frequent amongst men whose chief complaints had reference to the circulatory system. Besides complaining of breathlessness, pain in the chest, palpitation and giddiness, very many complained of a feeling of general exhaustion, headaches, insomnia, irritability of temper, loss of appetite and other more general symptoms. Anyone who has lived much with D.A.H. cases is impressed with the neurasthenic element in the vast majority; many even believe that the prime cause in all cases has to be sought in the central nervous system. This opinion is supported by the large numbers of cases of effort syndrome which occurred during the war, and by the fact that neurasthenic cases in civil life frequently complain chiefly of their cardiac sensations. Both in civil and military practice such patients, besides suffering from cardiac symptoms, are found to be tremulous; they look tired and exhausted and have an impaired digestion and a dirty tongue. In about 30 per cent. of all cases of D.A.H. the nervous manifestations dominated the picture, and a still larger percentage had symptoms of a lowering of the tone of the central nervous system. There was certainly a larger number of effort syndrome cases with nervous phenomena during the period of active fighting than after the armistice, and the number was still further reduced after demobilization.

The capacity of every human being to sustain with impunity both physical and mental strain is limited. Some have great capacity for sustaining either or both, but in the majority the breaking point is soon reached. The war called for extraordinary powers of both mental and physical endurance. During trench warfare, men had not to undergo unusual muscular effort while waiting to make the supreme effort of attack, but the period of waiting would be frequently spent in great physical discomfort and under great mental strain. Resting under such disadvantageous circumstances was a bad preparation for a physical and mental effort exceeding anything the individual had been previously called upon to undergo. After the effort had been made, further calls would be made for even greater endurance, and frequently on insufficient food and with no opportunity of recuperation by sleep. For instance, on one occasion 200 men and one officer were all that were left out of one battalion, and this remnant was ordered to dig a new trench. When at length relieved a very large percentage of those that remained complained of symptoms of cardiac distress on exertion during the weeks that followed. Such was a common experience. Many officers who had shown no fear, and who for months had been unconscious of any mental or physical distress under the circumstances incidental to trench life, stated that there came a time when they felt their hearts thumping during a bombardment or after a shell had burst particularly close to them. When the excitement was over the palpitation ceased, only to be repeated on the next occasion. Possibly on this second occasion palpitation persisted longer after the cessation of the disturbing influence. In other cases the tachycardia continued persistently and was intensified by exertion or further mental excitement. In this way a habit of tachycardia seemed to be established, and with it shortness of breath and pain in the left side of the chest on exertion. In those with smaller powers of endurance the amount of exertion and mental distress necessary to cause a breakdown was considerably less.

It has already been pointed out that 20 to 30 per cent. of those admitted to shell shock centres developed symptoms of the effort syndrome, usually after being some days in the centre. Many of these rapidly regained their nervous equilibrium when they arrived at a heart centre at the base, though the cardiac symptoms persisted. Such patients were usually able to return to the line. In others, however, the neurasthenic symptoms persisted in a milder degree and an air raid sent them flying all over the countryside. On the other hand, there were many men who had reported sick with pain in the chest, breathlessness and palpitation, who were not nervous and in no way belonged to the neurasthenic class. The symptoms in them had developed after an illness or after some period of unusual exertion and occasionally after some particular physical effort.

In any enquiry, after careful analysis of the past and present history and after thorough examination, there will always remain about 10 per cent. of the cases in whom no satisfactory explanation for the symptoms can be found. They seem to have become gradually worn out and exhausted by waiting in the line, loss of sleep, physical discomfort and occasionally improper or insufficient food.

It is abundantly clear from the symptoms and the physical signs of effort syndrome and its various possible causes that the effort syndrome is more of the nature of a group of symptoms than a clinical entity. The same phenomena are common in civil life and occur also in women and children, and further the symptoms may merely signify the onset of some organic disease such as pulmonary tuberculosis. The problem of causation has to be treated in the broadest possible manner, as the necessary physiological and pathological facts are wanting to complete the links in the chain of knowledge of the exact causation of the group of symptoms. For instance, the mode of production of pain in the chest under so many different clinical states is not understood as yet. The even simpler problem of the mechanism of the tachycardia is far from clear. It is not known whether it is a removal of control by inhibition, a continual speeding up by stimulation, or an endeavour to achieve in frequency that which cannot be achieved by force. Stress is laid on this aspect of the problem because some have approached the subject from too narrow a point of view, and many of the investigations which have been carried out have been in a very limited field. The true fact appears to be that everyone, at some time or other, suffers from the symptoms of D.A.H. or the effort syndrome. After unwonted exertion a perfectly normal person, or after ordinary exertion an individual in a lowered state of health from any cause, may suffer from pain in the chest, breathlessness and palpitation, or may have an attack of giddiness. After any illness the convalescent may suffer from these symptoms, and in addition may feel exhaustion after the smallest expenditure of mental and physical energy. The attempt to fit each case into one or other of the above categories can therefore only be imperfect, though by grouping the cases into them the proper course of treatment and disposal of each case is indicated.

Pathology.

With regard to the pathology of disordered action of the heart, certain investigations have been made, of which the following are the more important results. Pathological conditions in the two ductless glands, the thyroid and the suprarenal, have been investigated.

The hyperexcitability of the nervous system, tremors, tachycardia, and a proneness to sweating and flushing are common to both Graves' disease and the effort syndrome. They are, however, merely evidences of the overaction of the sympathetic nervous system and are common in various other conditions. In 517 cases of effort syndrome, Lewis found no enlargement of the thyroid in 483 cases; general enlargement in five cases; slight enlargement in four cases; one lobe enlarged in one case; one lobe slightly enlarged in three cases; isthmus enlarged in one case; isthmus slightly enlarged in five cases; and doubtful enlargement in 15 cases.

The thyroid gland was thus only palpably enlarged in 4 per cent. of cases. If the condition of D.A.H. was in many cases a mild form of Graves' disease, one would expect the more serious cases to cross the border line and become obvious instances of this disease. But in spite of the nerve strain of the war, there were comparatively few cases of exophthalmic goitre, and no case of the effort syndrome was ever seen to develop into the more serious disease.

Both excessive and diminished secretion of the suprarenal gland have been alleged to be the cause of disordered action of the heart. The evidences of hyperexcitability of the sympathetic nervous system and the rather higher range of systolic blood pressure in the cases suggest overaction of this gland. To test the theory the reaction of the circulatory system to intravenous injection of adrenalin chloride was investigated. It is known that patients suffering from Graves' disease tolerate the artificial injection of thyroid substance less readily than do normal persons. By the same analogy it was anticipated that intravenous injections of adrenalin would produce a result different from the injection of the same dosage into normal individuals. Fraser and Wilson concluded that the subjective sensations produced by intravenous injection were more marked in the patients than in the controls.

Others came to the same conclusion. Normal individuals, however, vary in their sensibility to such an extent that no deductions can be made from these experiments.

Fraser and Wilson in the same way injected apocodeine, a drug which stimulates ganglion cells on the vagus nerve, but obtained results which were inconclusive.

It has been suggested that the products of faulty metabolism, engendered in many cases by an infective process, cause some of the symptoms of the effort syndrome. Barcroft, Lewis and others brought forward evidence that there was a lack of " buffer salts " in the blood of such patients, and that the breathlessness was due to a hyperacid condition of the blood. Exercise causes an increase of lactic acid and carbonic acid in the blood which when uncompensated and unneutralized increases the hydrogen concentration of the blood with resulting stimulation of respiratory movements. Bainbridge, however, concludes that the chief " buffer salt " in the blood is sodium bicarbonate and that this is not lacking in the blood of patients with the effort syndrome. He suggests that the normal equilibrium between the reaction of the red cells and the plasma may be disturbed. But in whatever way the breathlessness may be produced, Lewis and his co-workers do not suggest that deficiency of " buffer salts " is responsible for the disturbances of the circulatory system.

Bainbridge suggests that the exaggerated circulatory and respiratory response to exercise, characteristic of the effort syndrome, may originate in some primary defect in the adjustments of the circulatory system which normally ought to occur during exercise.

It would appear that every gradation exists between the fully trained man on the one hand and the most severe case of effort syndrome on the other hand. In health, in response to the greater venous inflow consequent upon exercise, the heart dilates more fully, contracts more powerfully and increases its speed. It is suggested that in cases of effort syndrome the contractile power of the heart is diminished, and that the heart has to beat more frequently in order to bring about a given output per minute. Bainbridge points out that only in this way can the normal relationship between the demands of active organs for oxygen and the necessary supply of oxygen be maintained. It is suggested that intoxications of bacterial origin or any factor which will deprive the heart muscle of sufficient foodstuffs will impair the contractile power of the heart muscle. According to this line of argument the heart makes up by rapidity what it lacks in contractile force. This lack of contractile power may be produced temporarily by poisoning or malnutrition, may even be present from birth or have resulted from a sedentary life. Though this may be the explanation of the circulatory and respiratory phenomena in many cases, it is not of universal application. It has already been pointed out that there is an extraordinary difference in many cases between the rate of the heart when the patient is at rest and awake and the rate when he is at rest and asleep. The heart rate may be at all times fast during the waking hours, but the moment the patient drops off to sleep the rate may actually be halved in frequency. Since the body is at rest in both cases it seems that the mere reception of impressions from the outside world are alone sufficient to excite the heart to unnecessary activity, and this phenomenon suggests a purely nervous explanation of the effort syndrome.

To what extent, therefore, hyperexcitability of the central or peripheral nervous system would account for the rapidity of the heart rate and breathlessness requires investigation. The difference between the heart rate awake and asleep certainly suggests that nervous impulses alone may be sufficient to keep up an abnormal heart frequency. As far as respiration is concerned the nervous mechanism is often obviously at fault. Effort syndrome patients with neurasthenic symptoms are prone to breathe rapidly, shallowly and ineffectively, rates of 60 to 80 being frequently counted. It is extremely difficult to get a patient of this type to take a deep breath and almost impossible for him to stop breathing for more than a moment or two. He seems to have no nervous control at his disposal. Much of the abnormality in the breathing is obviously dependent on nervous influences and is not merely a compensatory effort to restore a lost balance between oxygen demand and oxygen supply. Indeed Haldane has shown that rapid shallow breathing is much less effective than is the ordinary rate for lung ventilation, and that it may in itself lead to actual deficiency of oxygen supply to the heart.

The onset of tachycardia and palpitation in men under repeated emotional disturbances suggests also that the continuing tachycardia in some cases is a persistence of a normal heart response to emotional stimuli.

It may be stated generally that tachycardia and dyspnœa are primarily dependent on many factors, some nervous and some toxic or metabolic. In the main, the abnormal responses in the circulatory and respiratory systems are largely an exaggeration of those which are normal and physiologically necessary in the natural response to exertion. In some, habits become established, and in others a weakness in one direction brings forth over-action in another. Further than this present physiological knowledge of biological processes does not go.

Diagnosis.

In order to distinguish between organic and functional cases of cardio-vascular disorders, Lewis states that the following are abnormalities of organic heart disease :—

(*a*) Aortic diastolic.
(*b*) Distinct over-distension of the veins of the neck.
(*c*) Definite signs of enlargement of the heart.
(*d*) An irregular heart action which is maintained on exercise, the heart-rate being high.
(*e*) A diastolic rumble at the apex.
(*f*) A basal or apical thrill. The thrill must be an unmistakable "purr"; a suspicion of thrill is insufficient.
(*g*) Widespread arterial disease or a persistent blood pressure of 180 or over in an elderly man, arterial disease or a persistent blood pressure of 160 or over in a young man.

He notes further that a systolic murmur most audible at the apex is not a sufficient sign of disease, even though the murmur is harsh and constant in all attitudes, but, if the murmur is associated with an unequivocal history of recent rheumatic fever, ten years, or occurs in a man of forty years of age, it is more difficult to overlook:

Treatment.

With regard to treatment it was early recognized that treatment in hospital, at any rate in war areas, was contra-indicated in patients of this class. It was a common experience that patients sent down the line with a diagnosis of V.D.H. and D.A.H. were prone to be in or on their beds the whole of the day. The discipline and graduated routine of exercise which is necessary in all types of this disability cannot, therefore, be so well carried out in a hospital as in a convalescent depot.

The first essential in proper treatment is the careful examination of each patient suffering from cardio-vascular symptoms, and a full understanding of his physical and mental history. Those found to be suffering from organic disease of the circulatory or any other system are suitably disposed of. The discharge from the army of cases of organic disease of the circulatory system ought invariably to be recommended. It is essential that evidences of any other organic disease should be carefully investigated, because the symptoms may arise from such diseases as tuberculosis. The remainder of the cases, about 80 per cent., will fall into one of the six categories of the effort syndrome, and the placing of patients in one or other of these groups suggests special lines of treatment and frequently indicates the prognosis.

It has been pointed out that the actual cause in any particular case is very elusive. Any infection must be sought and the patient treated accordingly. If there is fever, rest is necessary before the building-up process is commenced. Those who have some physical defect from birth will have to be put to work suitable to their physique. The causes which have been traced to a nervous breakdown must be removed when this is possible. Those who break down during active service in the line are more likely to recover when treatment is carried out away from danger, always bearing in mind that the greater the distance away a man gets from the line, the more difficult will it be to get him back there.

The patient is naturally alarmed about the state of his heart. Pain in the left side of the chest, breathlessness and palpitation are sufficient indications that there is something amiss with the heart. The patient will come to this conclusion whatever diagnostic label is attached to him. It is useless to attempt to tell a man with such symptoms that there is nothing the matter with his heart. Such only suggests to the patient ignorance on the part of the medical officer. It must be explained to the patient that he has no "heart disease" in the ordinary acceptance of that term. He will then enquire how it comes about that he should feel his heart beating so forcibly and should have pains over it, if there is nothing the matter with his heart. The patient can usually be satisfied if it can be explained to him that his nerves are too sensitive and that this causes the heart to beat too fast, and then that the sensitiveness of the nerves is due to the infection, the gassing, or the strain through which he has recently passed. He must be further told that his cure, though often prolonged, is certain in the end and that there is nothing in his heart which will lead to real disease or which will shorten or cripple his life. Most men are considerably relieved when their condition is explained to them in some such manner.

Graduated exercises are of benefit from both the prognostic and therapeutic points of view. The effects of exertion of various degrees on the individual form the surest guides as to fitness for work, and it is by gradual building up and training that a condition of fitness can be restored. The mornings should be occupied by graduated exercises under the supervision of special instructors. The exercises may be those of the physical training of recruits, and so arranged that the lowest grade includes only easy standing exercises, the second grade is intermediate in severity, and the highest grade includes exercises required by trained soldiers.

Lewis prescribed the following exercises at Colchester :—

Drill I. (15 minutes).

Heels raise and knees bend.
Arms sideways stretch, one arm upward, one arm downward stretch.
Trunk turning (feet apart).
Feet close and full open.
Trunk bending sideways.
Slow march.

Drill II. (15 minutes).

Heel raising and knee bending quickly.
One arm upward, one arm downward stretch.
Foot placing sideways.
Trunk bending sideways.
Trunk backward bend.
Slow march.

Drill III. (30 minutes).

This drill consisted of Drills I. and II.

Men on Drills II. and III. were sent for slow route marches of one to two miles in the afternoons, and were entitled to subsequent passes from the precincts of the hospital.

Drill IV. (30 minutes).

This drill consisted of Drill II., to which the following exercise was added :—
Arms forward bend.
Trunk turning.
Knee raising.
On the hands down.
Quick march.
Knee raising, quick mark time.
Slow march.

Drill V. (30 minutes).

Heels raise, knee bend, arm stretching sideways.
Head backward bend.
Arm swinging upward.
Trunk turning quickly.
Foot placing sideways.
Leg placing sideways.
Trunk bending sideways quickly.
Lying on the back down, leg raising.
On the hands down, arms bend.
Trunk forward bend, arm stretching sideways.
Knee raising, quick march.
On alternate feet hop.
Upward jumping.
Slow march.
Arm raising sideways, upward, sideways, downward.

Men on Drills IV. and V. were sent for longer route marches of four to five miles at an ordinary marching pace, and were entitled to longer passes from the grounds of the hospital. The men on Drill V. enjoyed additional privileges.

But graduated games under good instructors, particularly when accompanied by music, were infinitely superior to the set army exercises. The interest and pleasure of the patient are more easily secured by the former than by the latter.

Whenever possible, exercises and games should be conducted in the open air. In the afternoons route marches with a band should be arranged for the separate grades. All grades march off together, and the lowest grade returns by itself after a certain distance; the intermediate grade goes further before return, while the highest grade does a full one-and-a-half to two hours' marching with the band. Instead of the route march some are selected for games in the afternoon—football or cricket.

It was very noteworthy how badly the effort syndrome patient did army exercises or a route march without a band, and how much better his bearing was when his interest and emotions were excited during games and marching with a band.

While the patient is under treatment he should be well fed, and sleep should be procured by sedatives, if necessary.

An endeavour should be made to send a man, on discharge from treatment, to work suitable to his physical and mental capacity. This cannot be completely carried out in an army, though much useful work was accomplished in France in this direction by mutual co-operation between officers in charge of heart centres and assistant inspectors of drafts.

Prognosis.

It is only by a consideration of the results of treatment that a prognosis can be attempted. No man was considered fit for ordinary duty unless he had been on Grade 1 exercises and marches for 10 days.

The disposal of 1,000 men in 1917 after treatment in a cardiac centre in France, was as follows:—

Fit	580	or	58·0%
Permanent base duty—ordinary ..	172	,,	17·2%
Permanent base duty—light	44	,,	4·4%
Temporary base duty	86	,,	8·6%
Hospital	50	,,	5·0%
England—unfit	6	,,	0·6%
Unknown	17	,,	1·7%
Still in camp	45	,,	4·5%
	1,000	,,	100·0%

Those discharged "fit" were fit for the duty which they had left at the time of reporting sick; this did not always mean ordinary duty in the line.

The percentages of disposal of similar cases from the heart centre in Colchester in 1918 were as follows:—

Fit for general service	20%
Fit for hardening or labour	30%
Fit for light or sedentary work	30%
Permanently unfit	20%

During the war it was extremely difficult to check the accuracy of these estimates of fitness. The following figures are given by Lewis to show how 239 cases were classified on discharge from hospital and their disposition eleven months later.

On discharge from hospital.

Fit for general service	72
Likely to become fit for general service within three months	47
Light duty and unlikely to be fit for overseas within three months	20
Light duty and unlikely ever to be fit for service overseas	68
Sedentary work in the United Kingdom	32
	239

Condition eleven months after discharge from hospital.

Employed on full duty overseas	79
Employed on full duty in the United Kingdom ..	38
Employed in labour companies in the United Kingdom	23
Employed on light duty overseas	7
Employed on light duty in the United Kingdom ..	33
Employed on sedentary work in the United Kingdom	16
Still under medical treatment..	5
Discharged from the Service as permanently unfit ..	38
	239

Twenty-three thousand cases passed through the various heart centres in France between November 1916 and November 1918, and weekly nominal rolls of all cases were sent to the Boulogne centre. The number of cases who passed more than once through any heart centre was only 3 per cent. This figure was surprisingly small, even when it is allowed that many who went sick a second time with D.A.H. symptoms may have escaped the mesh of the cardiac centres.

Throughout the war the danger of allowing the symptoms of the effort syndrome to be taken too seriously were fully realized. Too great laxity always meant an unnecessary escape of men from military service. The main objects should always be, primarily, to prevent as far as possible the occurrence of the symptoms, and secondly, when they occur, to render men fit again to take their place in the army Prevention can be achieved in the infective group by a more prolonged convalescence and more graduated return to full duty. During convalescence the principles of treatment applicable to patients with the effort syndrome ought in reality to be applied to patients recovering from illness of any kind, because all are potential sufferers from the effort syndrome. All convalescents should therefore be systematically and gradually trained under medical supervision. If this were done universally it would be almost unnecessary to make special provision for the cardiac cases.

The knowledge of a man's capacity gained by the medical officers in convalescent depots should be passed on to the inspectors of drafts, and the latter should be largely guided by this information in allotting convalescents to the various types of duty.

Cardio-Vascular Disorders in Recruits.

The lessons which have been taught by the war in connection with effort syndrome have a special bearing on recruiting.

Recruiting for a small standing army is a very different problem from the enrolment of practically the whole manhood of the nation. The principles of selection are the same in both cases, but the selecting tests can be made much more severe when the recruits required are comparatively few. The tests are the history of the recruit's previous physical capabilities, a history of rheumatic fever, the position of the maximum impulse of the heart and the circulatory and respiratory response to an exercise test. These are the most important factors with which to form an idea of physical fitness. A simple test of physical fitness is the mounting of a chair ten times with each leg, counting the pulse before and immediately after the test, and again two minutes later, when the pulse ought to have fallen to the pre-exercise rate.

In future wars the same problems will arise as those which arose during the examination of recruits in 1914 to 1918. Whether special administrative arrangements will be necessary to deal with cases of effort syndrome amongst them will largely depend on the number of men required. In future campaigns some of the multitudinous causes of this disability will be prevalent, and the human machine will break down exactly as it has done in the past.

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INDEX.

Abrahams, Maj. : 213.
Aders, Dr. M. : 255 n.
Albuminuria : in influenza cases, 186 ; in nephritis, 496–7.
American Army : enteric fever in (Spanish-American War), 12 ; pneumonia in camps, 201.
American Civil War : 8, 147, 485 ; jaundice in, 374 ; cardio-vascular disorders in, 506.
Antimony : use in trypanosomiasis, 312 ; *administration of*, 313, 314 ; reaction to injections, 313 ; dosage of, 313–4.
Anæmia : post-malarial, 269 ; treatment to counteract, 276.
Army Medical Laboratory, Washington : 194.
Army Medical Service : need to consult, in planning a campaign, 10.
Arsenic : use of, for anæmia, 276 ; for malaria, 281 ; in trypanosomiasis, 312 ; *administration of*, 312–3.
Arthritis : as complication of dysentery, 73–4.
Atropine Test : used in enteric fever, 50.
Atrophy, Acute Yellow : similarity to spirochætal jaundice, 392.
Austro-Hungarian Army : cholera in, 116 ; trench fever in, 358.

Bacteriological Examination : for enteric bacilli, 51–3 ; for dysentery bacillus, 79–81.
Bacteriological Research : value of, in preserving efficiency of Army, 9 ; in enteric, 26–8 ; in bacillary dysentery, 67–9 ; in influenza, 191–5 ; in cases of purulent bronchitis, 214–5 ; in epidemic jaundice, 397–8.
Balfour, Lt.-Col. A. : viii ; his report on medical conditions in East Africa, 412–3.
Barraud, Lt. P. : 253.
Baths : need for further provision of, 9.
Belgian Army : suffers from relapsing fever in East Africa, 330.
Beri-beri : in Russo-Japanese War, 4 ; memoranda on, circulated in Mesopotamia, 428 ; definition, 430 ; regions in which endemic, *ib.* ; outbreaks during the war, *ib.* ; cause of these, *ib.* ; statistics of (Mesopotamia), 430–1 ; cases in Mesopotamia, 431, 441–2 ; these investigated, 431, 434 ; results of vitamine deficiency, 431–2, 435, 438 ; other toxic causes, 432 ; effects of investigations, *ib.* ; in Chinese porter corps, 432–3 ; in labour corps (France), 434 ; in British battalions from India, 434–5 ; other outbreaks, 435 ; ætiology, 435–42 ; diagram of sections of wheat, 436, 437 ; diagram showing milling of rice grain, *ib.* ; infective causes, 435 ; comparative value of foods affording protection against, 441 ; contributing causes, *ib.* ; effect of diet in intercurrent diseases, *ib.* ; predisposing causes, 442 ; experimental work, *ib.* ; morbid anatomy, 443–4 ; symptoms, 444–6 ; period of development, 444 ; types of, 444–6 ; prognosis, 446 ; diagnosis, 446–7 ; treatment, 447–8 ; diet, *ib.* ; preventive measures, 448 ; special hospitals for, *ib.*
Blackwater Fever : developed after malaria, 270 ; infected areas, 294, 295 ; prevalence during war, 294 ; susceptibility of white troops, *ib.* ; statistics of (Macedonia), 294–5 ; seasonal incidence, *ib.* ; ætiology of, 295–6 ; theories of causation, *ib.* ; morbid anatomy, 296–7 ; symptoms, 297–300 ; changes revealed by blood examination, 298–9 ; by examination of urine, 299 ; methods of determining severity of attack, *ib.* ; complications, 299–300 ; sequelæ, 300 ; susceptibility increased by attack, *ib.* ; mortality, *ib.* ; conditions minimizing chances of recovery, *ib.* ; prognosis, *ib.* ; diagnosis, 301 ; treatment, 301–3 ; *during convalescence*, 303 ; danger of neglect of mild attack, *ib.* ; preventive measures, *ib.* ; jaundice occurring in, 375.

Blake, Maj.: 194.

Bowlby, Sir A.: 8.

Boyd, Col. F. D.: 470.

Bradford, Sir J. Rose: 488, 490.

British Sanitary Mission to Serbia, 1915: composition of, 133; checks spread of typhus, 136–8.

Bronchitis: types of, occurring during war, 212.

Bronchitis, Purulent: in military camps, 177–8, 213, 214; symptoms, 212; incidence in France, 212–3; causation, 213; men most easily affected, *ib.*; organisms found on examination, 214; ætiology, 214–5; morbid anatomy, 215–7; illustration of lung tissue, 217; symptoms of cases in France and Flanders, 217–21; chart illustrating less acute case, 218; symptoms of cases in United Kingdom, 221–4; a typical case, 221–3; charts illustrating longer typical cases, 223–4; complications, 224; prognosis, 224–5; diagnosis, 225; treatment, 225–6; question of *contagion*, 226; *inoculation*, *ib.*

Brown, Capt. A. J.: 139.

Cane, Capt. E. G. S.: 431 n.

Cardio-Vascular Disorders: advances in knowledge regarding, 504; many affected with, after retreat from Mons, *ib.*; difficulties in interpreting signs of, *ib.*; Mackenzie's memorandum on, 504–5; special hospitals for, 505; centres in France, *ib.*; *value of these*, 506; statistics of, 506, 535; in American Civil War, 506; history of, in British Army, *ib.*; classification and nomenclature, 506–7; types, 508; organic disease, 508–10; percentage suffering from valvular disease, 508–9; functional disorders, 510–36; *symptoms*, 510–7; *ætiology*, 517–28; *pathology*, 528–31; *diagnosis*, 531; *treatment*, 531–4; *prognosis*, 534–6; in recruits, 536. *See also* Heart, Disordered Action of, and Heart, Valvular Disease of.

Catarrh, Naso-pharyngeal: its relation to cerebro-spinal fever, 149.

Cecil, Capt.: 194.

Cerebro-Spinal Fever: history, 147; statistics, *ib.*; dates of appearance, 148; ætiology, 148–50; incidence, 148; preventive measures, 148 n., 168–70; predisposing factors, 149; carriers, *ib.*, 168–9; overcrowding as cause of, 149–50, 168; exciting cause, 150; mode of infection, *ib.*; morbid anatomy, 150–1; symptoms and course, 151–60; incubation period, 151; complications, 154–5; types of, 155; *fulminating*, 155–6; *acute*, 156–7; *abortive*, 157; *suppurative*, *ib.*; *hydrocephalic*, 157–9; *recrudescent and relapsing*, 159; sequelæ, 159–60; prognosis, 161–3; period of invalidism, 161–2; pensionable disability, 162–3; condition of convalescents, 163; diagnosis, 163–4; treatment, 164–8; mortality, 165, 166; treatment centres, 166–7; prevention, 168–70; methods of disinfection, 169–70; chart illustrating fatality of, 167; chart illustrating relation of distance between beds to carrier rate, 169.

Chemical Warfare: jaundice arising from impure gas, 375.

Chick, Miss H.: 419, 421 n.

Chinese Porter Corps: outbreak of beri-beri in, 432; rations, 433.

Cholera: outbreaks during the war, 116; infected areas, *ib.*; *Mesopotamian* outbreak, 118–20; diagrammatic map of Cholera Creek, 117; causes of infection, 118–20, 121; statistics, 118–20; diagrammatic sketch of river steamer, 119; occurrence in Egypt and Sinai, 120–1; ætiology, 121–2; bacillus, *ib.*; carriers, *ib.*; symptoms, 122; incubation period, *ib.*; complications, *ib.*, 126; prognosis, 122–3; mortality, *ib.*; diagnosis, 123–4; treatment, 124–7; diet, 126; need for special medical units for treating, 127; prevention, 127–31; preventive inoculation, 127–8, 131; other preventive measures, 128–31; *in France*, 128–9; *in Salonika*, 129–30; *in Mesopotamia*, 130–1; *in Egypt*, 131; *in Sinai*, *ib.*

Christophers, Maj.: carries out malarial surveys (Mesopotamia), 256.

Commissions: British and American, discoveries in trench fever, 360–1, 361.

Committees: W.O. trench fever, 9, 358, 362; Medical Research, 149, 199, 442 n., 505; Medical Investigation, 1917, 358; American Research, on trench fever, *ib.*, 362, 368; Medical Advisory, Mesopotamia Enquiries, investigates scurvy, 1916, 416; W.O. Sanitary, 1916, investigates beri-beri (Mesopotamia), 432; on Mesopotamian ration, 439; on pellagra, 470; on soldier's heart, 506.

Conferences: W.O., on vaccine for influenza, 206.

Conjunctivitis: as complication of dysentery, 74.

Convalescent Depôts: for dysentery patients, 75, 91.

Convalescents: from dysentery, 89.

Copeman, Dr. S. M.: 440.

Cummins, Capt.: 232.

Davy, Maj. P. C. T.: 139.

de Grey, Earl: 506.

Dengue: identification with phlebotomus fever, 353–4.

Diarrhœa: at Suvla Bay, 396.

Dietary: of Indian soldier, unscientific, 6–7, 411; faults in (Mesopotamia), 410; anti-scorbutic additions to, 420–1; influence of various, on pellagra, 480–3.

Diets: in enteric fever, 53; in dysentery, 84; in cholera, 126; in blackwater fever, 303; fresh meat juice, in scurvy, 418; hospital, in scurvy, 426–7; in beri-beri, 447–8; in nephritis, 502.

Disease: inefficiency from, exceeds killed and wounded, 1; statistics of, *South African and Russo-Japanese Wars, ib.*; *Great War*, 1–2, 3–4; average number of days' treatment, 3 n.; comparison with Russo-Japanese and South African Wars, 4–5; wastage of minor, 7; main groups of these, *ib.*; 44 per cent. preventible, 8; lessons of Great War, 9–10; at Suvla Bay, 395–7.

Dropsy, Famine: description of, 450; early accounts, 450–3; in Madras jails, 1864, 451; in Indian famine, 1877–8, 451–2, 452; in Lushai expedition, 1875, *ib.*; in siege of Paris, 1870–1, *ib.*; probably differs from epidemic dropsy, 453; first appearance in Great War, Lille, October, 1914, *ib.*; epidemic in Central Empires, 453–4; in prison camps in Germany, 453; among Turkish prisoners, 454; relative sex incidence, *ib.*; mortality, *ib.*, 464; ætiology, 455–6; exciting cause underfeeding, 455; other contributory causes, 455–6; symptoms, 456–9; pathology, 459–62; possible physical causes, 460–1; concurrent diseases, 462, 463; diagnosis, 462–4; prognosis, 464; treatment, 464–5; prevention, *ib.*

Dudgeon, Col.: 235.

Dysentery: 4, 9–10; average number of days' treatment for, 2 n.–3 n., 76–7; statistics, 3; incidence of, 5–6; diagnosis, 5; meaning of term, 64; study of, during the war, *ib.*; incidence of, 1914–18, *ib.*; types of, 65; among prisoners of war in Germany, 67; diet, 84; cases of suspected, segregated, 89–91; convalescents, 89, 91; examination of suspicious cases, 90; special accommodation, 90–1; precautions against transmission, *ib.*; forms of, other than bacillary and amœbic, 104–5; malarial, 105; conditions easily mistaken for, *ib.*; routine management of, to ensure adequate treatment, 105–6; at Suvla Bay, 396.

Dysentery, Amœbic: meaning of term, 92; comparison with bacillary, 92–3; ætiology, 92–5; prevalence, 92; incidence, 93–4; morphological research, 94; predisposing causes, 94–5; morbid anatomy, 95; symptoms, 95–7; incubation period, 95–6; causes of death, 97; prognosis, 97–8; assessment of pension in case of, 97; diagnosis, 97–8; treatment, 98–101; complications, 100–1; prevention, 101–3; carriers, *ib.*; method of transmission, 103.

Dysentery, Bacillary: characteristics, 65; prevalence in war areas, 65–6; case mortality, 66; invalidism due to, *ib.*; ætiology of, 66–9; predisposing circumstances, 66–7; outbreaks in France, *ib.*; bacteriology of, 67–9; morbid anatomy, 69–72; symptoms, 72–5; incubation period, 72; clinical types, 73; *fulminating*, *ib.*; *gangrenous*, *ib.*; *chronic*, *ib.*; complications, 73–5; sequelæ, 74; prognosis, 75–7; disposal of, patients, 75, 89–91; fitness for convalescent depôt, how determined, 75; cases unfit for duty, 76; cases entitled to pensions, *ib.*; danger of, when complicated with other fevers, *ib.*; diagnosis, 77–81; *laboratory*, 78–80; *sero-*, 81; treatment, 81–6; *of chronic*, 85; *of complications*, 85–6; prevention, 86–91; carriers, 86–7; transmission *by flies*, 87; *by contaminated water*, 87–8; *by dust*, 88; prophylactic inoculation, *ib.*

East Prussian Campaign, 1806: 8.
Elliott, Col. T. R.: viii.
Emetine: treatment of amœbic dysentery with, 98.
Endocarditis: an infective factor in V.D.H., 509-10.
Enteric Fever: 4; *statistics* (Great War), 3, 4, 15–7; previous wars, 11–2; comparison between South African and Great Wars, 4–5; measures to prevent, 5, 55–6, 58–60; value of inoculation, 5, 56; definition of term, 11; effect of inoculation, 15, 19, 22, 24, 32, 43–5, 56–8; diagnosis, 15–7; *clinical*, 49–51; *laboratory*, 51–3; mortality, 18–22; *comparative* of the three groups, 19–20; ætiology, 22–8; influence of environment, 22; carriers, 23–4, 48; immunity from, 24; relative incidence and mortality in British and Indian races, 24–5; effect of age, 26; predisposing factors in war, *ib.*; exciting causes, *ib.*; bacteriological research, 26–8; morbid anatomy, 28–31; complications, 44, 47; mixed infection of different groups, 45; association with other diseases, 46; prognosis, 46–7; invalidism, 47–9; duration of treatment, 47–8; discharge from military service after, 48; diagnosis, 49–53; treatment, 53–5; prevention, 55–60; comparative statistics (protected and unprotected), 57; relative immunity conferred by inoculation in the three groups, 58; jaundice in, 401-4; *charts illustrating*, 401, 402, 403.

Flexner Bacillus: causes dysentery, 68; bacteriological examinations for, 80–1; carriers, 86–7.
Flexner, Dr.: 378.
Flies: as carriers of enteric fever, 23; of dysentery, 87, 103.
Food Poisoning, Diseases due to: differentiated from enteric fever, 51.
Foster, Col.: 156.
Franco-German War: enteric in, 12.
French Army: 345; enteric in (Tunis operations), 12; malaria in (Italy), 257; blackwater fever in (Eastern campaign), 295; trench fever in, 358; jaundice in, 378; famine dropsy in, 1528, 450.
French, Col.: 213.
Fruit: grown in Mesopotamia, 417; precautions against infections from raw, 418.

Gas Gangrene: 8; pathological laboratories investigate, 9; jaundice resulting from, 376.
Gases, Poison: effect of, on the heart, 52, 524; on the lungs, *ib.*
German Army: enteric fever in (Franco-German War), 12; cholera in (Great War), 116; typhus in, 145; blackwater fever in (E. Africa), 294; trypanosomiasis in, 305; relapsing fever in (E. Africa), 330; trench fever in, 358; jaundice in, 378; rations in Turkey, 482; physical training of, recruits, 522.
Gerrard, Capt.: 454.
Glover, Capt.: 149.
Greig, Maj.: 121.

Hargreaves, Sgt.: 258.

Heart, Disordered Action of: 359; after enteric, 48–9; in trench fever cases, 366, 369; difficulty of nomenclature, 507; symptoms attributable to inherent physical defect, *ib.*; descriptive terms, 510; symptoms of, not necessarily organic, *ib.*; manifestations of, 510–1; physical signs, 512–3; rate of heart, 513; irregularities of heart, 514–5; diastolic and systolic murmurs, 515; significance of systolic murmurs, 515-6; blood pressure, 516; circulatory and nervous symptoms, 517; cause of disability in, cases of pre-war onset, *ib.*; cases occurring after enlistment, 518; influence of previous diseases in comparison of cases with and without effort syndrome, 519; age incidence, *ib.*; lesser contributing factors, 520; enlargement of thyroid in, 520–1; effect of poison gases on, 521; a result of mental disturbance, *ib.*; other predisposing causes, 521–2; pathology of, 528–31; distinction between organic and functional cases, 531; treatment, 531–6; graduated exercises for, 532–4; value of graduated games, 533–4; disposal on discharge from treatment, 534–5; results of treatment, *ib.*; prevention of occurrence and recurrence, 535–6.

Effort Syndrome, prime factors underlying, in, 521–2; cases due *to poor physique*, 522; *to previous infections*, 523–4; *to poison gases*, 524; *to sudden exertion*, 524–5; nervous phenomena in, 525–6; cases of, due to physical and mental strain, 526–7; problem of causation, 527–8; in connection with recruiting, 536.

Heart, Valvular Disease of: varieties of, 508–9; previous history of rheumatic fever in cases of, 508; usually of pre-war origin, 509; need of discharging patient with, from army, 510, 531; treatment, 531–4.

Hepatic Abscess: *see* Liver Abscess.

Herringham, Maj.-Gen. Sir W.: viii.

Hill, Professor L.: investigates outbreak of scurvy in prisoners of war camp, 413.

Hill, Sir R.: 420 n.

Hine, Lt.-Col. T. G. M.: 170.

Hodgson, Col. E. C.: 253.

Horrocks, Col.: 439.

Hume, Miss M.: 419, 421 n.

Hume, Col. W. E.: 188, 490.

Hunter, Col. W.: in charge of British Sanitary Mission to Serbia, 133.

Huts: mosquito-proof, 245; method of rendering tick-proof, 343–4.

Influenza: statistics, 174–6; in France, 174–5; world-wide nature, 175; in Mesopotamia, 175–6, 206; symptoms amongst troops in United Kingdom, 176–86; epidemics, 176–8; summer epidemic, 1918, 176–7; incidence of "pneumonic" (*q.v.*), cases in autumn epidemic, 178; mortality, 176; infectivity, *ib.*; symptoms amongst troops in the field, 186–91; incubation period, 186; course of summer epidemic, 188; course and symptoms of autumn epidemic, 188–90; complications, 190–1, 209; pathology, 191–5; effect of vaccination, 193; question of immunity, 195; morbid anatomy, 195–205; diagnosis, 205; prognosis, *ib.*; treatment, 205–9; preventive measures, 205–8; *on Japanese cruiser "Nukata,"* 207 n.; inoculation, 206–7; *statistics of results*, 207; occurring with jaundice, 376–7; charts illustrating variability of temperature in, 182–4.

Influenza, Pneumonic: description of, 178–9; types, 179; symptoms and course, 179–86; heliotrope cyanosis, 181; its nature and causation, 181–2; complications, 186.

International Commission of Hygiene: 129.

Italian Army: malaria in, 257.

Japanese Army: 24; sickness in Russo-Japanese War, 4.
Jaundice: attributable to enteric fever, 41; a complication of influenza, 190–1; a symptom in many diseases, 374; area of epidemics, *ib.*; pathological research, 374–5, 378–81, 386; maladies in which, may occur, 375–6; types of, 375–8; in cases of influenza, 376–7; in enteric fever, 401–4; *charts illustrating*, 401, 402, 403; *symptoms*, 401–2; *description of cases*, 402–3; *diagnosis*, 404; *pathology*, 404; theories of origin, *ib.*
Jaundice, Epidemic (Camp): symptoms, 395, 398–400; catarrhal, infected localities, 395; accounts of, *ib.*; statistics of, 395–7; carried to new localities, 397; ætiology of, 397–8; course of epidemic, *ib.*; association between incidence of, and of other diseases, 397; bacteriological research, 397–8; incubation period, 398; question of specificity of infection, *ib.*; course of infection, 399; description of cases, 400; *charts illustrating*, 399; *cause investigated*, 400.
Jaundice, Spirochætal: micro-organism identified, November 1914, 374, 378; cause of, 375; in British Army, 378; ætiology of, 378–81; illustration of *SPIROCHÆTA ICTERO-HÆMORRHAGIÆ*, 379; ditto, in blood of guinea-pig, 380; antiserum for, 380–1; symptoms, 381–6; incubation period, 381; course, 382; description of cases, 383–5; *charts illustrating*, *ib.*; diagnosis, 386, 392–4; morbid anatomy, 386–92; illustrations of section of liver, 387, 388, 389, 390; illustrations of section of kidney, 391; differentiation from other diseases, 393–4; prognosis, 394; treatment, 394–5.

Kaye, Dr. H. A.: 162.

Laboratories: pathological investigations regarding gas gangrene, 9; mobile bacteriological research, work of, 9–10; Army, their blood-film examinations (malaria), 236.
Lauder, Capt.: 139.
Laundries: need for more, 9.
Ledingham, Lt.-Col.: compiles malaria statistics (Mesopotamia), 257 n.
Leishman's Stain: 272.
Lelean, Lt.-Col. P. S.: 470.
Lewis, Dr. T.: studies in cardio-vascular disorders, 505.
Lice: disease resulting from infestation by, 8; as cause of typhus, 133–4; life history of, 134; as cause of relapsing fever, 316; *how conveyed by*, 318; proved cause of trench fever, 360; *method of infection*, 360–1.
Lime Juice: no anti-scorbutic value (Mesopotamia), 419; freshly prepared in India, *ib.*
Lister Institute, The: 421 n.
Liver Abscess: relationship with amœbic dysentery, 100; symptoms, 100–1; diagnosis, 101; treatment, *ib.*

Mackie, Maj.: 257.
MacLean, Capt. H.: 486.
Malaria: 4, 10; figures for, 1916–18, 3, 227; difficulty of prevention in war, 6; responsibility of, for disease pensions (1920), *ib.*; *in Macedonia*, 227–45; *map illustrating area occupied by British*, 228; effect of climate on, 227; description of country with reference to, problem, 228–30; effect of advance on, 230–1; admissions, 1916–18, *ib.*; extent of infection, 231, 235; chief carriers, 232–5; reason for greater prevalence in valleys, 233–4; association of one mosquito with one type of, not justified, 233; outbreaks, 234,. 240–1; cases among hospital personnel, 234; relative incidence of benign and malignant tertian, 234–5; *chart illustrating incidence*, 236; results of army laboratories' examinations, 236–7; infections in civil population, 237–8, 242–3; mortality, 241–2; arrangements for outbreak inadequate, *ib.*; predisposing causes, 242; forms of, parasites, *ib.*; anti-mosquito measures, 243–4, 246; *their results*, 244–6.

Malaria—*continued.*

In Army of the Black Sea, 246–7; consequences of lack of protection, 247; Russian Government's schemes for prevention, *ib.*

In Palestine and Egypt, 247–53; statistics of, 247–8; areas of infection, 248; conditions favouring, in different sectors (Palestine), *ib.*; means of combating, 249–50; incidence, 251–3; effects of advance, 252–3; relative incidence (Eastern war areas), 253.

In E. Africa, 253-5; infected localities, 254, 255; insufficient precautions against, 254, 255; incidence and mortality, 254–5.

In Cameroons, 255.

In Mesopotamia, 255–7; admissions, 255–6; effect of climate and topography on, 256; surveys, *ib.*; statistics of incidence, 256–7.

In Italy, 257–60; infection in front line, 257; on lines of communication, 257–8; at Taranto camp, 258–9; anti-mosquito operations, *ib.*; comparative difficulty of these, in different war areas, 260.

Causes of death, 264–5; morbid anatomy, *ib.*; symptoms, 265–70; tertian periodic pyrexias, 265–6; quartan, 266; subtertian infections, *ib.*; cases easily confused with, *ib.*; types of malignant tertian, *ib.*, 267–9; *symptoms,* 266–7; *how produced,* 267; diseases simulated by, 267–9, 270–1; sequelæ, 269–70; danger of co-existing diseases, 270; diagnosis, 270–3; *special units for,* 271–2; treatment, 273–80; *of convalescents,* 275–6; *of serious cases,* 277–80; disadvantages of intra-muscular administration of quinine in, 277–9; quinine poisoning, 280–3; treatment of malarial invalids, 283–8; invaliding of chronic cases, 283; types invalided, 283–4; duration of invalidism, 284; anti-relapse treatment, 284–5; measures to render infected battalions fit for service, 285–7; results of these, 287; as cause of blackwater fever, 296; jaundice occurring in, 375.

Marjoribanks, Maj.: 418.

Marmite: a prophylactic against beri-beri, 440.

Marris, Capt.: 402.

Martin, Lt.-Col. C. J.: 443.

Maude, Gen.: 120.

McCarrison, Lt.-Col. R.: proves wide-reaching effects of vitamine deficiency diet, 422, 442.

Medical Research Council: 76, 284, 354, 370, 502.

Medicine, Clinical: high standard of, in war, 10.

Melville, Lt.-Col. H. G.: consulting physician, Mesopotamia, 431; his recommendations for the prevention of beri-beri, 432.

Meningitis: occurring in influenza, 186.

Meningococcus: exciting cause of cerebro-spinal fever, 150; types, *ib.*

Mercury: used in treatment of relapsing fever, 340.

Mitchell, Maj. T. J.: viii.

Morphological Research: in amœbic dysentery, 94.

Mosquitoes: breeding-places (Macedonia), 230–1, 231–2; types, *ib.*; relative distribution, 232–3; chief carriers of malaria, *ib.*; suggested difference in carrying powers, 233; association of certain, with one type of malaria not justified, *ib.*; how infected, 236; infectivity of, 237–8; period of hibernation, 238–9; survival powers of larvæ, 239; development of presporozoite cysts in winter, 239–40; effects of quinine on, 240; anti-, measures, 240, 245, 249; *their results,* 243–5; prevalence in Tiflis-Baku area, 246; types *in Egypt,* 247; *in Palestine,* 249–50; observations on development of (Palestine), 253; in E. Africa, 255; in Mesopotamia, 256, 257; destruction of (Italy), 258–9; types in Italy, 259; experiments in infectivity, 259–60; list of, found in war areas, 260–2.

Mosquito Nets: 245.

Myalgia: 8, 359.

Napoleonic Wars: 147.
Nephritis: statistics, 3; occurs in American Civil War, 8, 485; a complication of influenza, 190; war, 485; incidence of, 486–7, 489; in association with *respiratory disease*, 486–7, 489, 490; *with cerebro-spinal meningitis*, 487; *with infected wounds, ib.*; ætiology, 487–91; causation, 487–8; difficulty of diagnosis, 487; influence of previous attack of renal disease, 488; as a complication, 488–9; troops most liable to attack, 489–90; freedom of Indian troops, 490–1; morbid anatomy, 491; symptoms, 491–500; *in hæmorrhagic type*, 492–3; *in dropsical type*, 493; clinical course, 494–5, 499–500; pathology, 495–8; complications, 498–9; results of urine examination, 499; comparison between war, and, of civil life, 499–500; prognosis, 500–2; mortality, 500; statistics showing results of treatment, 500–1; chronic or recurrent cases, 501; duration of treatment, *ib.*; diagnosis, 502; treatment, 502–3.
Neuritis, Multiple: 446–7; of toxic origin, mistaken for beri-beri, 435; how distinguishable (from beri-beri), *ib.*
Nicholson, Capt.: 377.

Œdema, Famine: *see* Dropsy, Famine.
Œdema, Hunger: *see* Dropsy, Famine.
Œdemas: clinical, types of, 459–60; defects in capillary walls giving rise to, 460; other possible causative factors, 460–1; frequent early sign in nephritis, 494.
Opium: to be avoided in bacillary dysentery, 82; use of, in phlebotomus fever, 355.

Paratyphoids: incidence of, 1914–18, 13; distribution at outbreak of war, 15; how developed in new areas, *ib.*, 17; comparative incidence of, and typhoid, 15–7; case mortality, 20; *compared with typhoid, ib.*, 21, 32; *in the East*, 21; *of, A. and B. compared*, 21–2; relative incidence of, B. in British and Indian troops, 25; cause of infection, 26; morbid anatomy, 29–31; incubation period, 32; symptoms, 32–40; convalescence, 40; complications, 40–1, 43–4; clinical types, 41; *dysenteric, ib.*; *biliary, ib.*; *rheumatic*, 42; *respiratory, ib.*; *influenzal, ib.*; *septicæmic, ib.*; diagnosis, 49, 49–53; charts illustrating, A., 35–7; charts illustrating, B., 37–9.
Park, Capt.: 453.
Pasteur, Col.: 190.
Pathological Research: in trench fever, 360; in jaundice, 374, 378, 381.
Pathologists: *American*, their discoveries regarding trench fever, 9; their investigations of pneumonia, 200-2; *Japanese*, their research in jaundice, 374, 378.
Patrick, Capt.: 205.
Pellagra: first recorded, 1735, 470; locality, *ib.*; outbreak among Turkish prisoners, *ib.*; committee on, 1918, *ib.*; incidence and distribution, 470–7; chart illustrating, 471; map illustrating, 472; monthly incidence among prisoners of war, 470; absence of, among British and Indian troops, 471; prevalence in Egyptian Labour Corps, 471–2; German and Austrian prisoners not infected, 472; ante-bellum prevalence slight, 473; affected districts, *ib.*; largely of pre-capture onset among prisoners, *ib.*; incidence in Turkish Army, 474; question as to cause, 474–5, 478–9; seasonal prevalence, 475; *chart illustrating*, 474; relation between incidence and labour, 476; *chart illustrating*, 475; need for early treatment, 476; statistics of prisoners of war admissions, 477; symptoms, *ib.*; treatment, *ib.*; morbid anatomy, 478; death usually due to supervening infection, 478; ætiology, 478–84; due to deficiency in biological protein value of diets, 479; mal-assimilation of food in, 479–80; influence of various dietaries on, 479–83; chart illustrating dietetic values, 480; incidence in German and Turkish prisoners of war contrasted, 481; reasons for German freedom from, 481–2; among Armenian refugees, 483; *chart illustrating incidence among*, 483; physiological processes in production of, 484.

Pensioners : numbers suffering from cardio-vascular disorders, 506 ; incidence of V.D.H. among, 509.

Pensions : for disabilities due to enteric, 49 ; of dysentery patients, 76, 97 ; granted after cerebro-spinal fever, 162 ; after relapsing fever, 338 ; after trench fever, 369.

Pfeiffer's Bacillus : alleged causative agent in influenza, 191–5.

Phlebotomus Fever : definition of, 345 ; geographical distribution, *ib.* ; in Macedonia, *ib.* ; ætiology of, 345–8 ; carried by sand-flies, 345–6 ; predisposing causes, 346 ; exciting cause, *ib.* ; how transmitted, 346–7 ; illustration of *Phlebotomus papatasii* and larva, 347 ; symptoms, 348–53 ; incubation period, 348 ; charts illustrating temperatures during, 350–2 ; convalescence, 353 ; question of immunity, *ib.* ; diagnosis, 353–4 ; identification with dengue, 353 ; distinction from other diseases, 354 ; treatment, 354–6 ; *duration of*, 355 ; preventive measures, 355–6.

Physique : comparison between British patients at heart centre, and German prisoners, 522.

Pike, Surg.-Gen. : his report on medical conditions in E. Africa, 412–3.

Pleurisy : in influenza cases, 196.

Pneumonia : in influenza cases, 196 ; outbreaks after measles and influenza in American camps, 200–2 ; pathological investigation of, 201 ; morbid anatomy, 202–3, 204 ; types, 203–4 ; jaundice in lobar, 377.

Pneumonia, Broncho- : *see* Bronchitis, Purulent, and Pneumonia.

Priestly, Maj. : 139.

Prisoners of War : dysentery among, in Germany, 67 ; cholera among Russian, 116 ; Austrian, spread typhus in Serbian, 135–6 ; typhus among Austrian, 136, 140 ; typhus in German, camps, 138–9 ; scurvy *among Turkish*, 411 ; *among Russian*, 412 ; *among German, 1917*, 413 ; rations in, camps, *ib.*, 481 ; famine dropsy among, in Germany, 453 ; poverty of rations, 455 ; outbreak of pellagra among Turkish, 470, 477 ; this largely of pre-capture onset among, 473 ; Kantara labour camp, 476, 478–9 ; relative incidence of pellagra among German and Turkish, 481–2.

Pyorrhœa : in cases of scurvy, 423.

Pyrexia of Uncertain Origin : 8 ; trench fever mistaken for, 359.

Pyrexias : statistics at Suvla Bay, 396.

Quinine : effect of, on mosquitoes, 240 ; protection afforded by prophylactic, 246 ; treatment in malaria, 273–4 ; prescriptions, 274–5 ; methods of administration, 277–9 ; excretion of, by urine, 280 ; tests for presence of, *ib.* ; preparations of, 280–1 ; dangerous effects of, 281–3 ; blindness, 281–2 ; a factor in precipitating blackwater fever, 296 ; opinion on use of, in blackwater fever, 202.

Rationing, Principles of : fighting forces educated in, against deficiency diseases, 428.

Rations : of Indian troops, *in Mesopotamia*, 6-7, 409, 438 ; *and in India*, 409 ; lack of anti-scorbutic vitamines in, 410 ; of German prisoners of war, 413 ; field, in Mesopotamia, 415–7, 438–9 ; addition of anti-scorbutic articles, 414 ; fresh meat issued in, 418 ; of Chinese Porter Corps (Mesopotamia), 433 ; German, for prisoners, 455 ; value of British, Ottoman and European (enemy), in calories, 480–1 ; German Army, in Turkey, 482.

Rats : carriers of jaundice, 378–9.

Relapsing Fever : characteristics, 316 ; types, *ib.*, 322 ; infection, how transported, 316 ; ætiology of, 316–8 ; conditions favouring, 316–7 ; epidemics in Serbia, 317 ; chart showing course of, *ib.* ; exciting cause, 317–8 ; illustration of *Sp. recurrentis*, 318 ; infection, how conveyed, 318 ; morbid anatomy, 319 ; symptoms, 319–22 ; chart of typical, 320 ; incubation period, 319 ; convalescence, 322 ; complications, *ib.* ; prognosis, 322–3 ; varying intensity of epidemics, 322 ; period of invalidity, 323 ; immunity, *ib.* ; diagnosis, 323–4 ; diseases easily confused with, 324 ; treatment, 324–6 ; preventive measures, 326 ; aundice n 377. *See also* Jaundice, Spirochætal.

Relapsing Fever, E. African : occurs in tropical Africa, 329 ; account of, in Carrier Depôt Hospital, Dar-es-Salaam, 329–30 ; races liable to attack, *ib.* ; amongst Belgian troops, 330 ; ætiology, 330–2 ; illustrations of insect vector, 331 ; method of infection, 332 ; morbid anatomy, *ib.* ; symptoms, 332–8 ; incubation period, 332 ; illustrations of infection, 333 ; charts illustrating, 334, 335, 336, 337 ; course of, 334–7 ; observations of Manson and Thornton, 335 ; involvement of different organs, 337 ; complications, 338 ; prognosis, *ib.* ; treatment of convalescents, *ib.* ; diagnosis, 338–9 ; presence of other diseases excluded by blood examination, 339 ; treatment, 339–44 ; *charts illustrating*, 341–3 ; preventive measures, 340–4.

Renal Disease : few cases in British Army prior to February 1915, 485 ; examination of troops to detect, 486 ; results of this examination, 488 ; previous attack of, predisposes to nephritis, *ib.*

Respiratory Affections : prevalence in France and Flanders, 212 ; statistics from Meerut Stationary Hospital, 1914 and 1915, 213.

Rheumatism : 8, 359.

Rice : polished, a beri-beri producer, 433, 440 ; Chinese preference for polished, 433, 440.

Rickettsia Bodies : 361 ; description of, *ib.* ; in connection with trench fever, *ib.*

Roaf, Prof. H. E. : 484.

Robertson, Col. J. C. : his reports on anti-malarial work at Taranto, 260 n.

Rogers, Sir L. : his treatment for cholera, 122.

Rolleston, Sir H. : his observations on cerebro-spinal fever, 149.

Ross, Sir R. : his experiments in effects of quinine, 285.

Russian Army : 24 ; enteric fever (Russo-Turkish War), 12 ; cholera among prisoners of war in Germany, 116.

Russo-Japanese War : statistics of sick and wounded, 1 ; comparison with Great War, 4 ; enteric fever in, 24 ; scurvy in Port Arthur, 425 n.

Russo-Turkish War : enteric in, 12.

Salvarsan : for treating relapsing fever, 324–5, 340 ; jaundice in, poisoning, 377.

Sand-flies : carriers of phlebotomus fever, 345–6, 347 ; *illustration of*, 347 ; how rendered infective, 346–7 ; distribution of, 347 ; description of, 347–8 ; larvæ, 348 ; repellents of, 355–6 ; methods of destruction of, 356.

Sanitary Measures : disease preventible by, 8 ; possible reforms in, 9 ; (necessity of) for preventing enteric fever, 58–60.

Scurvy : in Mesopotamia, teaches lessons in dietary, 6–7 ; a deficiency disease, 409 ; incidence in Mesopotamia, 1916–18, *ib.* ; causative factors, 409–10, 411, 414 ; outbreaks among Indian troops, 410 ; *in France, 1915*, 411 ; in South African Native Labour Corps, 1918, *ib.* ; in British troops, 1915, 411-2 ; in N. Russia, 1919, 412 ; period of development, *ib.*, 422 ; amongst civil population (Murmansk) 412 ; amongst natives in E. Africa, 412–3 ; in Great Britain, 414 ; ætiology of, 414–22 ; chart illustrating admissions, 418 ; preventive rations in N. Russia, 420–1 ; effects of climate on, 421 ; other predisposing causes, *ib.* ; influence of race, *ib.* ; experimental work on, *ib.* ; morbid anatomy, 422 ; symptoms, 422–5 ; groups of, 422 ; progress, 423–5 ; mortality, 425 ; prognosis, *ib.* ; diagnosis, 425–6 ; simulated by malingerers (Mesopotamia), 425–6 ; treatment, 426–7 ; preventive measures, 427 ; special hospitals for (Mesopotamia), *ib.* ; convalescent camp for, *ib.* ; memoranda on, circulated in Mesopotamia, 428.

Sera : anti-dysenteric, 82–4 ; storage of, 83–4 ; for prophylactic inoculation against dysentery, 88 ; M.R.C., for cerebro-spinal fever, 165.

Serbian Army : cholera in, 116 ; precautions against cholera, 129 ; conditions in retreat, 138.

Sheppard, Capt. A. L. : 423, 427 n. ; his notes on early diagnosis of scurvy, 427.

Shiga's Bacillus: discovered 1897, 67; causes dysentery, 67–8; bacteriological examination for, 80–1; carriers, 86; in flies, 87; in water, *ib.*
Shore, Capt.: 195.
Sick and Wounded: statistics (South African and Russo-Japanese Wars), 1; proportions of (Great War), 2; *estimate of, in R.A.M.C. Training Manual, ib.*
Skin Diseases: sick wastage due to, 7–8; in South African War, 8.
Sleeping Sickness: *see* Trypanosomiasis.
Small pox: 4.
Smith, Miss A. Henderson: 419.
Soltau, Col. L.: 8; analyses admissions for disease in a casualty clearing station, 7, 359; his report on influenza, 187.
South African War: statistics of sick and wounded, 1; comparison with Great War, 4; skin diseases in, 8; enteric in, 11; jaundice in, 374.
Spanish-American War: enteric in, 12.
Spirochæta ictero-hæmorrhagiæ: micro-organism of jaundice, 378; description of, 379–80; illustrations of, 379, 380.
Spirochætosis: *see* Relapsing Fever.
Spironema: species of, 317–8; illustration of *Sp. recurrentis* in human blood, 318.
Sprawson, Lt.-Col. C. A.: investigates cases of beri-beri (Mesopotamia), 434.
Stammers, Lt.-Col. G. E. F.: 133, 144.
Starling, Prof.: 440.
Stevenson, Capt. A. J.: 419, 424; investigates cause of scurvy, 412; experiments in N. Russia, 420–1.
Stevenson, Maj. H. W.: investigates beri-beri (Mesopotamia), 432.
Supplies: difficulties of transport (Mesopotamia), 410; transport improved, 417.

Taylor, Capt.: 231.
Tetrachlorethane: poisoning from, causes jaundice, 374, 377–8.
Tick: cause of relapsing fever, 317, 331; description of, *ib.*; illustrations of, *ib.*; habitat, 331–2; method of determining infection of, 339.
Tick Fever: *see* Relapsing Fever, E. Africa.
Tidy, Capt. H. Letheby: observes cases of dysentery (France), 75.
Todd, Capt.: 188.
Topeley, Capt. W. W. C.: 133.
Trench Fever: statistics, 8; first observed in Great War, *ib.*; pathological research in, 8–9, 360–2; report of committee on, 9; definition, 358; areas of incidence, *ib.*; other titles of, *ib.*; history of, *ib.*; incidence, 359; made notifiable, 1918, *ib.*; cases wrongly diagnosed, 359; statistics, 359–60; ætiology of, 360–2; first recognized, 1915, 360; dissociated from enteric, *ib.*; incubation period, 362; symptoms, 362–8; charts illustrating, 364, 365; course of, 367–8; chronic cases of, *ib.*; period of incapacitation, 368, 369; invaliding, 368–70; after-effects, 369; disposal of convalescents, *ib.*; duration of invalidism, 370; prognosis, 370–1; persistence of infection, *ib.*; diagnosis, 371; treatment, 371–2; preventive measures, 372; no epidemic of, in United Kingdom, *ib.*; not associated with nephritis, 492–3.
Trench Foot: observed in E. Prussia, 1806, 8; measures to prevent, *ib.*; statistics of, 1917, *ib.*
Trinitrotoluene: poisoning from, causes jaundice, 374, 377.
Trypanosoma: different strains of, 305–6.
Trypanosomiasis: characteristics of, 305; confined to Africa, *ib.*; statistics of, *ib.*; cases among British forces, *ib.*; ætiology of, 305–7; causative organism, 305–6; types of, 306; carriers, *ib.*; infected areas, *ib.*; morbid anatomy, 307; symptoms, 307–11; charts illustrating, 308, 309; incubation period, 307–8; complications, 310; course of, 310–1; prognosis, 311–2; difficulty in pronouncing a case cured, *ib.*; diagnosis, 312; treatment, 312–5; prophylactic measures, 314–5.
Tsetse Fly: carrier of trypanosomiasis, 306; habitat, 306–7.
Turkish Army: lack of anti-mosquito measures in, 249; relapsing fever in (Mesopotamia), 316; pellagra resulting from war in, 474.

Typhoid: incidence of, 1914–18, 13; distribution at outbreak of war, 15; how developed in new areas, *ib.*, 17; comparative incidence of, and paratyphoid, 15–7; case mortality, 19–20; *compared with paratyphoid*, 20, 21, 32; cause of infection, 26; clinical features, 31–2; incubation period, 32; complications, 43–4; diagnosis, 49–53.

Typhus: 4; most widespread epidemic of the war, 133; British Sanitary Mission to Serbia, *ib.*; ætiology of, 133–4; history of, 133; means of infection, 133–4; distribution, 134–42; infected areas, 134; in Russia, 134–5; in Poland, 135; in Turkey, *ib.*; in Austria, *ib.*; *cause of* (Serbian epidemic), 136; *chart showing course of epidemic*, 136; *statistics of*, *ib.*; *inadequate hospital accommodation*, *ib.*; preventive measures *allied*, 136–8, 144; *chart showing*, 137; *enemy*, 144–5; *lessons in*, 145; subsequent incidence in Serbia, 138; in prisoners of war camps in Germany, 138–9; in Greece and Roumania, 139; statistics of, in British Army, 139–40; in Portugal, 139; seasonal incidence, 140; symptoms, 140–2; incubation period, 140; clinical features, 141–2; *chart showing*, 141; diagnosis, 142; prognosis, 143; mortality in Serbia, *ib.*; treatment and prevention, 143–5; in German armies, 145.

Vaccines: triple, for enteric, introduced January 1916, 15, 56; *its effect*, 19, 21–2, 24, 56–8; *its contents*, 56; therapeutic use of, in enteric, 55; treatment for dysentery, 85; for prophylactic inoculation against dysentery, 88; cholera, 128, 130; influenza, 193, 206.

Vegetables: grown in Mesopotamia, 417; precautions against infections from raw, 418; value of germinated lentils in scurvy, 420.

Vermin: prominence of infection by, 8; need for more destroyers, 9.

Vidal, Capt.: 139.

Vitamine, Anti-beri-beri: nature of, 436; distribution in food-stuffs, 438; rations lacking in (Mesopotamia), *ib.*; *addition to, of factors containing*, 439; comparative value of foods containing, 441.

Vitamine, Anti-scorbutic: foods containing, 414; methods to avoid destruction of, in cooking, *ib.*; dietaries deficient in, 414–5; value of fresh meat, 418; relative value of lime and lemon juices in, 419; value of Indian dried fruits in, 419–20; discovery of value in, of germinated lentils, 420.

Water: bacilli in subsoil, 22–3; cause of enteric fever, 23; contamination of, by dysentery organisms, 87–8, 103.

Water Supply: means of securing pure, 58–9; defective, causes cholera (Mesopotamia), 118–9, 120; in Sinai desert, 131.

Watts, Lt.-Col. R. C.: 253.

Weil's Disease: *see* Jaundice, Spirochætal.

Wellcome Bureau of Scientific Research: 379.

Willcox, Col. W. H.: 419, 427 n., 439; consulting physician (Mesopotamia), 431; his recommendations for the prevention of beri-beri, 432.

Wilson, Capt. J. A.: 496.

Wilson, Prof. W. H.: his theory on cause of pellagra, 479.

Wiltshire, Dr. H.: 423.

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